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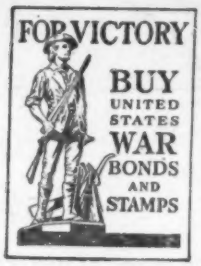

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BACTEROIDES INFECTIONS*

An Analysis Based on a Review of the Literature and a Study of Twenty Cases

WILLIAM E. SMITH, M.D.,† AND MARIAN W. ROPES, M.D.‡

BOSTON

THE gram-negative anaerobic bacilli that do not bear spores have been grouped together in a genus to which the name "Bacteroides" has been assigned.[1] There are many reports of human infections caused by Bacteroides, but the occurrence of such cases is not widely appreciated. During the last four years, 20 cases have been seen at this hospital (Table 1). On the basis of cases reported in the literature and those seen here, an attempt will be made to describe the clinical aspects of these infections, with the purpose of calling attention to the various conditions in which Bacteroides infection should be suspected.

TABLE 1. *Bacteroides Infections Seen at the Massachusetts General Hospital, 1939–1943.*

TYPE OF INFECTION	NO. OF CASES	RESULT	
		DIED	SURVIVED
Septicemia arising from tonsillar abscess ..	1	1	
Septicemia arising from abdominal abscess	1		1
Meningitis arising from chronic otitis media	5	1	4
Peritonitis arising from ruptured appendix	3		3
Peritonitis arising from salpingitis	1		1
Liver abscess after colectomy	1	1	
Kidney abscess	1		1
Chronic otitis media	2		2
Chronic cervicitis	2		2
Chronic prostatitis	2		2
Skin infection	1		1
Totals	20	3	17

In general, it may be stated that organisms of the Bacteroides group are common inhabitants of mucous membranes, particularly of the nasopharynx,[2] the gastrointestinal tract[3] and the cervix and vagina.[4] From these sites they may invade the tissues, the blood or the body cavities by extension of local inflammatory processes. If the blood stream is invaded, metastatic abscesses frequently occur, notably involving the lungs, pleural cavities, liver and joints. The occurrence of metastatic abscesses makes the prognosis extremely grave.

The classification of species within the genus Bacteroides is discussed at the end of this paper. It should be noted that the Bacteroides do not include the anaerobic bacilli of the Dialister and Fusiformis groups, which are at present preserved as separate genera,[1] the one because of the small size of the organisms composing it, the other because of the characteristic pointed shape of its members. Detailed data concerning the many known strains of Bacteroides have been compiled by Weinberg, Nativelle and Prévot.[5] Recently, Dack[6] has published a review of the Bacteroides of medical importance. In studies of strains recovered in this laboratory, a form of bacterial reproduction different from simple fission and associated with the production of anaerobic pleuropneumonia-like colonies as variant growth forms (L-type variation) has been encountered in certain instances. These studies have been presented elsewhere.[7-11]

BACTEROIDES SEPTICEMIAS

Bacteroides septicemias usually arise following throat infections, otitis media and mastoiditis, surgery or infections of the large bowel or genitourinary tract and war wounds. Etiologically, these septicemias may be divided into two groups. The first and more frequent are the cases caused by the *Bacteroides funduliformis* group of organisms, markedly pleomorphic bacilli characterized by the formation of large bodies (spheres) and filaments on cultivation in artificial mediums. These cases frequently develop metastatic abscesses and carry a high mortality. Pus from the abscesses is usually thick, greenish yellow and somewhat foul but not putrid. The organisms are present in large numbers and may readily be detected in smears as small gram-negative bacilli. The second, and less frequent, group of cases are caused by *Bact. fragilis* or other nonpleomorphic Bacteroides. These cases usually run a less fulminating course, with less tendency to

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the formation of metastatic abscesses. Their prognosis is less grave, only 3 of 8 reported cases having had a fatal termination.[12]

Following Throat Infections

Excellent clinical and pathologic studies of *Bact. funduliformis* septicemias following throat infections have been presented by Lemierre[13] and by Pham Huu Chi.[14] Among 16 cases, 13 were fatal. The close similarity of Case 1 of the present report and that recently described by Brown, Williams and Herrell[15] to the cases reported by these authors is striking. The cases usually occur in previously healthy persons between twenty and thirty years of age. The onset is sudden, with a chill and high fever, usually on the fourth or fifth day of a pharyngitis, tonsillitis or peritonsillar abscess. The local infection in the throat may appear mild or severe. Chills may recur frequently. Multiple abscesses in the lungs, liver and joints and a serous or purulent pleurisy may develop. Jaundice is frequently observed. A moderate anemia, with a red-cell count of 3,800,000 to 2,800,000, and a polymorphonuclear leukocytosis, with a white-cell count of 14,000 to 22,000, are encountered. In acute cases death may follow within a week.

Joint metastases occurred in 8 of 12 cases, chiefly involving large joints, such as the elbow (4 cases) scapulohumeral (4 cases), knee (3 cases) and hip (1 case).[14] Except for the sternoclavicular joint, which was involved in 2 cases, the smaller articulations were spared. Recovery without ankylosis occurred in 1 case following incision and drainage of two joints and a spontaneous resorption of the effusion in a third. *Bact. funduliformis* was seen in smears of the pus obtained from these joints and was recovered in cultures. Joint involvement — of the hip — was also seen in 1 of the 2 fatal cases of septicemia with *Actinomyces necrophorus* reported by Cunningham.[16] According to Dack,[6] this organism may be identical with *Bact. funduliformis*.

Following Chronic Otitis Media and Mastoiditis

Bacteroides septicemias arising from chronic otitis media and mastoiditis have been reported. Of 2 cases due to *Bact. fragilis*, 1 resulted in recovery.[17] In 1 case due to *Bact. funduliformis* there developed osteomyelitis of the femoral head with abscess in the hip joint.[18] This patient recovered after drainage of the joint and sequestrectomy of the femoral head. It could not be determined whether the infection had arisen in the bone and extended into the joint or vice versa. From a case reported by Rist,[19] it appears that Bacteroides infection of a joint may destroy the cartilage and invade the bone or spread through the synovial tissues to present itself as a subcutaneous abscess.

Following Surgery of Large Bowel

A series of *Bact. funduliformis* septicemias following surgery of the large bowel has been reported from the Mayo Clinic. In 1934, Beaver, Henthrone and Macy[20] described a fatal case following colostomy for carcinoma of the rectum. In the same paper they described another case, which, in the light of Lemierre's cases,[13] appears to have originated from an upper respiratory infection. In 1937, Dixon and Deuterman[21] reported 5 proved cases and 1 presumptive case, all of which followed operations for carcinoma of the large bowel. A fatal termination ensued in the 5 cases in which *Bact. funduliformis* was cultivated from the blood. Multiple abscesses in the liver and lungs were observed at autopsy. Pyelophlebitis was found in 3 cases. The authors concluded that *Bact. funduliformis* septicemia should be suspected when postoperative convalescence is interrupted by a chill, fever, profuse sweating and jaundice. In Case 4 of the present series, Bacteroides were recovered in mixed culture from a liver abscess in a man dying of sepsis after colectomy. In Case 2, a Bacteroides septicemia arose from an abdominal abscess.

Following Infections of Genitourinary Tract

Bacteroides septicemias arising from the genitourinary tract have been observed in cases of septic abortion and of puerperal sepsis and in postoperative infections. *Bact. fragilis* was cultivated from the blood of 2 women with chills and fever following abortion.[17, 22] Metastatic abscesses did not develop, and both women recovered within a week. *Bact. fragilis*, however, has been cultivated from the blood in a fatal case of post-partum septicemia with liver abscess.[23] Two fatal cases of Bacteroides septicemia following operations have been reported by Thompson and Beaver,[24] who[25] have since identified the strains from both cases as *Bact. funduliformis*. Both cases occurred in elderly men, one of whom had suprapubic drainage for carcinoma of the bladder, and the other of whom underwent prostatectomy and removal of stones from the bladder. Chills, fever and leukocytosis appeared ten to eighteen days postoperatively, and death occurred after five to six days of fever. Multiple abscesses were found in the lungs.

Following Infected Wounds

Bacteroides septicemias arising from wounds were observed by Bogdán[26] in Hungary during World War I in soldiers with gunshot wounds involving bones, that is, deep wounds in which conditions were favorable for the development of anaerobic infections. In some cases infection around the wound seemed slight, whereas in others it progressed to gangrene or thrombophlebitis. The onset of septicemia was marked by the appearance of chills and

fever in soldiers who had appeared to be making a satisfactory convalescence. There was severe pain over the region of the liver, with radiation to the right shoulder. Jaundice was frequently noted. The course of the disease was punctuated by the development of metastatic abscesses in the liver, lungs, spleen and joints. Of 24 patients, 16 died after illnesses of about two weeks. These Bacteroides wound infections appeared to spread from one patient to another, since all occurred in two nearby hospitals and appeared in rapid succession until the transmissibility of the disease was recognized and greater precautions were taken in treatment of the wounds.

Buday[27] demonstrated that the etiologic agent in a similar series of wounded soldiers with septicemias was a Bacteroides, which has since been known as *Bact. pyogenes anaerobius*. The presence of serum in the medium was necessary for growth. Buday's bacillus was closely similar to *Bact. funduliformis* and was placed by Weinberg et al.[5] in that group.

Case 1.* A 22-year-old man was admitted on June 6, 1939, with a complaint of chills, fever, headache and sore throat of 14 days' duration. He had previously been in good health. Several days after the onset of the illness, a tonsillar abscess had broken down spontaneously. On admission, the temperature was 105.6°F., the pulse 125, and the respirations 28. The patient appeared to be very ill. Both tonsils were hypertrophied and covered with a profuse, thick, white exudate. There were enlarged lymph nodes at the angles of the jaw. The remainder of the physical examination was not remarkable.

The patient was desperately ill throughout the hospital course and exhibited a septic temperature, with daily excursions between 101 and 106°F. The pulse ranged between 110 and 150. He was given sulfanilamide for 4 days, with a resulting blood level of 13.3 mg. per 100 cc., but the drug was discontinued because of the appearance of jaundice, which became steadily deeper. On the 5th day, fluctuation was observed over the right acromioclavicular joint. Incision and drainage of this joint yielded 60 cc. of thick, creamy-yellow pus containing innumerable gram-negative bacilli and 530,000 white cells per cubic millimeter, 95 per cent of which were polymorphonuclear leukocytes. The left arm became swollen and painful, and crepitus due to gas in the tissues was noted. An extensive abscess developed involving the entire left elbow and upper arm. This was incised and drained on June 19. The patient died on June 22, a month after the onset of his illness.

On admission, the white-cell count was 15,500, with 82 per cent neutrophils. The red-cell count was 4,600,000, and the hemoglobin 90 per cent. The urine gave a ++ test for albumin. Despite repeated transfusions, the red-cell count fell to 1,940,000. The serum bilirubin level (van den Bergh reaction) rose from 10.1 mg. per 100 cc. (biphasic) on June 9 to 31.8 mg. (direct) on June 20.

Bacteriology. Blood cultures and cultures of pus from the right acromioclavicular joint were made in meat tubes during life. Gram-negative bacilli were cultivated from both sources. Broth cultures exhibited diffuse turbidity, with production of gas and a foul odor. Colonies on ascitic-agar plates were smooth, yellowish white and convex with an entire edge and attained a diameter of 1.0 to 1.5 mm. after 48 hours' incubation. Colonies on blood-agar plates were nonhemolytic. The organisms were markedly pleomorphic in size and shape, producing long filaments and large, round bodies. They were strictly anaerobic. Neither spores, capsules nor motility was seen. A young pleuropneumonia-like growth (L-type variation) was observed beneath and near some of the bacterial colonies.[11] Owing to its marked pleomorphism, this strain has been placed in the *Bact. funduliformis* group.

*We are indebted to Dr. L. Dienes and Dr. E. R. Sullivan for permission to report this case.

Case 2. A 26-year-old nurse delivered a normal baby (her first child) on September 30, 1941. The day after delivery she had a chill with a temperature of 105°F. There was spasm and tenderness in the left lower quadrant. On the following day, 250 cc. of foul, thin pus gushed from the rectum. Sulfadiazine was given for 4 weeks, with a dosage of 6 to 3 gm. a day. The temperature ranged between 101 and 103°F. for 1 week, after which it remained normal for 4 days. Following this, there was another chill and 4 more days of fever. The patient completely recovered and was discharged on November 1, 1941. The infection was believed to have originated from an abscess that ruptured into the bowel.

The white-cell count ranged between 13,250 and 11,800, with 88 per cent neutrophils. The red-cell count remained about 3,500,000, and the hemoglobin about 65 per cent. The urine was not remarkable. The blood level of sulfadiazine ranged from 4.6 to 10 mg. per 100 cc.

Bacteriology. One half to 1 cubic centimeter of blood taken on two occasions while the patient was having a chill was inoculated into four meat tubes. Growth was obtained on both occasions. Diffuse turbidity occurred, with the production of a small amount of gas, which did not have a particularly foul odor. Colonies on ascitic agar plates were smooth, grayish white and convex with an entire edge and attained a diameter of 1 mm. after 48 hours' incubation. Colonies on blood-agar plates were nonhemolytic. The organisms were small gram-negative bacilli 1.5 to 2 microns in length and quite regular in size and shape. They did not produce large bodies, and L-type variation was not observed. They were strictly anaerobic. Neither spores, capsules nor motility was seen. Owing to its nonpleomorphic character, this strain was placed in the *Bact. fragilis* group.

Cases 1 and 2 bear out the impression gained from the literature of the greater severity of septicemias due to the pleomorphic Bacteroides (*Bact. funduliformis* group) than of those due to Bacteroides of uniform morphology (*Bact. fragilis* group). Sulfanilamide did not appear of value in Case 1 during the four days it was given. The prompt recovery in Case 2 was probably due to spontaneous perforation and drainage of the abdominal abscess. It is impossible to determine whether sulfadiazine was of value, since comparable recoveries in previously cited cases of septicemia due to nonpleomorphic Bacteroides occurred without drug treatment.

The jaundice that led to the discontinuance of the drug in Case 1 may well have been a result of the infection. In fact, jaundice is so frequently seen in *Bact. funduliformis* septicemias that its occurrence should be regarded as evidence in favor of liver abscess rather than drug intoxication, especially when other signs of drug intoxication are lacking.

Gas in the tissues, as noted in Case 1 and in a previously cited case[16] is occasionally a point of value in differential diagnosis. All the strains encountered in this study produce gas in cultures.

The treatment of Bacteroides septicemias corresponds to that of other septicemias arising from focal infections and producing metastases. Appropriate surgical procedures, such as drainage of pus and ligation and excision of affected veins, are the important factors. A case has already been cited of recovery following drainage of metastatic joint abscesses and another following sequestrectomy of an infected bone. Rib resection and drainage was followed by recovery of 2 out of 3 patients with *Bact. funduliformis* empyema occurring after upper

respiratory infection.[28] Buday[27] noted that the only recoveries in his group of soldiers occurred when liver abscesses perforated the lung and drained through the bronchi. There is a recent report of recovery from postanginal *Bact. funduliformis* septicemia following excision of the internal jugular vein on the side of the affected tonsil.[29] None of these patients received sulfonamides.

Sulfonamides have been used in 2 reported cases. A patient with *Bact. funduliformis* liver abscess recovered following sulfathiazole therapy and surgical drainage.[30] Another with postanginal *Bact. funduliformis* septicemia was treated with sulfapyridine and recovered.[15] This drug was said to have affected the course favorably, but the major factor was apparently rib resection with drainage of an empyema. There is therefore no adequate clinical evidence that sulfonamides are of value. Animal experiments, however, indicate that sulfanilamide inhibits the spread of abscesses produced by subcutaneous injections of Bacteroides cultures[31] and effectively controls septicemias produced by intravenous injections.[32]

Bacteroides Meningitis

Between 1898 and 1939, at least 11 cases of Bacteroides meningitis were reported. Brain abscesses were present in 4 of these. All the cases were fatal, and all arose from chronic otitis media except one of brain abscess that occurred in a patient with bronchiectasis. Between 1940 and 1943, 5 cases of Bacteroides meningitis have been seen at the Massachusetts Eye and Ear Infirmary. All arose from chronic otitis media that had extended into the mastoid or labyrinth. Brain abscess occurred in 2 cases.

The onset of Bacteroides meningitis is acute, and the symptoms and course are similar to those of meningitides caused by other pyogenic organisms. In smears of spinal fluid, the organisms may be seen as small gram-negative bacilli lying within the cells or extracellularly. They may be mistaken for influenza bacilli. Diagnosis depends on cultivation of the organisms, and meat tubes enriched with ascitic fluid have proved highly satisfactory for this purpose. In one patient, organisms could not be found in direct smears of the spinal fluid but were recovered in cultures. Such a case might have been regarded as so-called "sterile meningitis" if anaerobic cultures had not been repeatedly made. Cultures should be held at least two weeks before being discarded as sterile.

In view of the uniformly fatal outcome of all previously known cases, it was of considerable interest that 4 of the 5 patients in this series recovered. Early and adequate surgical drainage, repeated lumbar punctures and the use of intravenous fluids and transfusions appeared to be the major factors in aiding recovery, but there was evidence that sulfadiazine was a useful adjunct in a patient who had three separate episodes of meningitis, each of which subsided promptly on administration of the drug. Detailed reports of these cases have already been published.[33, 34]

Bacteroides Peritonitis

Bacteroides are among the most frequent organisms in human feces, being present in 90 per cent of stools,[3] often in greater numbers than the colon bacillus.[35] It is therefore to be expected that Bacteroides will be present in the peritoneum when leakage from the bowel has occurred. In the classic studies of Veillon and Zuber,[36] various species of Bacteroides were recovered from the peritoneum in a score of cases of gangrenous appendicitis, and these authors concluded that Bacteroides were the most frequent organisms in this condition.

There are many subsequent accounts of strains isolated from the peritoneum.[8] Most strains were recovered at autopsy, but it should not be inferred that the cultivation of Bacteroides from the peritoneum necessarily confers an unfavorable prognosis. We have cultivated them during life from 5 patients, only 1 of whom died. Among 3 patients with gangrenous appendicitis yielding Bacteroides, 2 recovered uneventfully. Case 5 is cited as an example. The third (Case 3) developed a subdiaphragmatic abscess that yielded a pure culture of Bacteroides. As described in the section on septicemia, thrombophlebitis and invasion of the blood stream by Bacteroides with formation of liver and lung abscesses may arise from abdominal infections. In Case 4, the patient died, having developed an abdominal abscess and a liver abscess following colectomy.

Peritonitis resulting from leakage from the bowel is of course a mixed infection. It was therefore of interest to encounter a case of peritonitis from which Bacteroides were isolated in pure culture. In this patient (Case 6), the peritonitis arose from a salpingitis and, although extensive, subsided within a few days. Clinically, it simulated gonococcal peritonitis.

Case 3. A 53-year-old laborer was admitted on June 27, 1941, with a ruptured appendix and peritonitis. Following operation, he remained in the hospital for 8 months with a pelvic abscess that continued to drain pus through a fecal fistula. Jaundice appeared in November but gradually cleared. In December, a subdiaphragmatic abscess developed on the left and was drained surgically. Treatment included sulfadiazine and sulfathiazole, as well as transfusions. The patient improved slowly and was discharged to a nursing home in March, 1942.

The white-cell count ranged from 5400 to 13,400, and the red-cell count from 2,900,000 to 4,700,000. The serum bilirubin level (van den Bergh reaction) in November was 14.6 mg. per 100 cc. (biphasic).

Bacteriology. Pus from the ruptured appendix and fecal fistula yielded Bacteroides, *Escherichia coli*, alpha-hemolytic and nonhemolytic streptococci, *Staphylococcus aureus* and several species of Clostridia — the flora of the colon. Abdominal fluid withdrawn in November because of ascites yielded many colonies of Bacteroides and anaerobic diphtheroids and a few colonies of alpha-hemolytic streptococci. This fluid was not purulent. Pus from the subdiaphragmatic abscess yielded a pure culture of Bacteroides. The Bac-

teroides from this case possessed morphologic and cultural characteristics similar to those of the strain from Case 2 and were regarded as *Bact. fragilis*.

Case 4. A 63-year-old factory worker had an ileotransverse colostomy on April 27, 1941. A right colectomy for removal of carcinoma of the ascending colon was done 11 days later. A right-gutter abscess and fecal fistula developed. The temperature, which had ranged between 100 and 102°F., suddenly began to spike to 103 and 105°, and tenderness was noted over the anterior right costal margin. Sulfapyridine therapy (6 gm. a day) was instituted, but the patient died 1 week after the onset of the spiking fever — 23 days after the colectomy.

Autopsy. In the right flank there was a large abscess cavity into which fecal material was leaking from the blind end of the transverse colon. The right lobe of the liver contained a multiloculated, necrotic abscess filled with greenish-yellow pus of foul odor. No evidence of thrombosis was found in the portal circulation. There was an area of bronchopneumonia in the right lower lobe.

Bacteriology. A blood culture taken during life grew alpha-hemolytic streptococci. Pus from the abscess yielded *Esch. coli*, *Staph. aureus* and nonhemolytic streptococci. Anaerobic cultures were not made. Culture of the heart's blood at autopsy yielded diphtheroids that were regarded as contaminants. Pus from the liver abscess yielded an abundant growth of *Bact. fragilis* in mixed culture with *Proteus vulgaris* and nonhemolytic streptococci.

Case 5. A 37-year-old chauffeur was admitted on May 31, 1941, with abdominal pain of 4 days' duration. At operation a necrotic appendix was found in the center of a large abscess cavity. Sulfanilamide was placed in this cavity, and cigarette drains were inserted. Sulfapyridine (6 gm. a day) was given for 5 days. The patient improved steadily and was discharged well after a stay of 1 month in the hospital. A fecal fistula healed solidly 1 month after discharge.

Bacteriology. Pus taken at operation from the appendiceal abscess yielded an abundant growth of *Bact. fragilis*, *Esch. coli* and a few colonies of alpha-hemolytic streptococci.

Case 6.* A 30-year-old, unmarried woman was admitted on December 21, 1940, because of lower abdominal pain of 18 hours' duration. There was boardlike rigidity in both lower quadrants of the abdomen. The temperature was 100.5°F., and the pulse 90. Sulfathiazole (1 gm. every 4 hours) was given for 6 days. The temperature fell to normal within 3 days, the pulse remaining around 90. X-ray examination showed many dilated loops of small bowel, suggesting obstruction, and exploratory laparotomy was performed 3 days after admission. The bowel was diffusely coated with creamy-yellow pus, and a large amount of pus was found in the pelvis. There was no perforation or obstruction of the bowel. The right tube appeared normal. There was hydrosalpinx on the left. The abdomen was closed without drainage. The patient appeared quite well after 1 week.

Total hysterectomy, bilateral salpingectomy and right oöphorectomy were done 2 weeks later. The right tube was filled with milky fluid and purulent exudate. The right ovary contained many cysts filled with milky fluid. The patient made an uneventful recovery and was discharged well on February 9.

The gonococcus complement-fixation test was negative. The white-cell count fell from 28,700 on admission to 9300 several days later, with a corresponding fall in neutrophils from 92 to 61 per cent. The red-cell count rose from 3,860,000 to 4,870,000. The urine gave a + test for albumin but was otherwise negative.

Bacteriology. Cervical cultures were negative for gonococci but yielded an abundant growth of aerobic pleuropneumonia-like organisms. Aerobic cultures of pus obtained from the peritoneum at the first operation remained sterile, but on anaerobic horse-serum-agar plates and semisolid rabbit-serum agar *Bact. funduliformis* was isolated. On anaerobic plates a few pleuropneumonia-like colonies also developed. Subcultures of this strain of Bacteroides showed that it produced anaerobic pleuropneumonia-like (L) colonies as variant growth forms. The organisms may have been present in the tissues in the L form, since direct smears of the pus revealed no ordinary bacilli, but the polymorphonuclear leukocytes were distended by masses of small granules. Photographs and studies of this bacillus and its relation to the L forms have been published elsewhere.[11]

*We are indebted to Dr. L. Dienes and Dr. J. V. Meigs for permission to report this case.

As stated above, the cultivation of Bacteroides from the peritoneum may be expected in cases in which there has been leakage from the bowel and should not necessarily confer an unfavorable prognosis. The participation of these organisms in intra-abdominal infections should be borne in mind, however, and anaerobic blood cultures should be made in cases of peritonitis exhibiting septic fever or jaundice.

Localized Bacteroides Infections

Like other natural inhabitants of mucous membranes, the Bacteroides may give rise to or participate in localized infections in or near these sites, being found either in pure culture or together with other organisms. As described in preceding sections, generalized Bacteroides infections may arise from such localized processes.

An extensive but neglected study on the bacteriology of otitis media was made in 1900 by Rist,[37] who concluded that the Bacteroides played an important role in chronic suppurative otitis media, particularly in cases with foul-smelling discharge, whereas ordinary pyogenic cocci were the most important agents in acute otitis. We have cultivated Bacteroides from 2 patients with chronic suppurative otitis media.

Bacteroides have been recovered from various urinary infections in males and females, from cervicitis and Bartholin abscesses[4, 38] and from the lochia of women with post-partum fever.[39] We found them in mixed culture in 3 women with chronic endocervicitis and in 2 men with chronic prostatitis. *Bact. funduliformis* was recovered in pure culture from the pus of a kidney abscess (Case 7). A discussion of the distribution of these organisms in the healthy female genital tract and in genitourinary infections is given at the end of Rist's paper.

Bacteroides have been cultivated from lung abscesses.[40] Dack[6] believes that they may be of importance in chronic ulcerative colitis, either as primary agents or as secondary invaders. They have been found in abscesses on the hands of persons who had scratched the skin while working with material from animals infected with *Actinomyces necrophorus* (presumably *Bact. funduliformis*).[5, 6] Such abscesses are usually small and self-limited. We repeatedly recovered *Bact. funduliformis* in mixed culture with staphylococci or streptococci from a severe case of suppurative hydroadenitis of nineteen years' duration. At the time this patient was seen, multiple draining sinus tracts were present on the buttocks and many healed scars were seen on the face, in the axillas and over the chest and back.

Bact. fragilis was isolated in this laboratory from the eye and cervix of a patient with conjunctivitis and arthritis who was regarded as possibly suffering from Reiter's disease. These organisms were recovered from the eye in pure culture, but could not be isolated from samples of blood or fluid from an affected joint or from other cases of Reiter's disease. Gonococci were not demonstrable. Until the cause of this disease is known, the etiologic significance of Bacteroides cannot be established.

CASE 7. An 83-year-old man was admitted on August 7, 1942, with a complaint of aching pain in the left flank of 3 weeks' duration. A large, fluctuant mass was felt in the left upper quadrant of the abdomen. X-ray examination revealed renal calculi on the left. The temperature was 100°F., and the white-cell count 16,000. The urine contained large numbers of red and white cells. A large perinephric abscess was found at operation. About 1000 cc. of foul yellow pus was drained from the abscess, and the kidney was removed. The abscess had eroded into the wall of the splenic flexure of the large bowel but had not penetrated the mucosa. Following the operation, sulfadiazine (2 gm. a day) was given for 10 days. A fecal fistula developed, but the patient did well and ran an essentially afebrile course. He was discharged 2 months after admission. The fistula closed within 5 months.

Bacteriology. Pus from the kidney abscess inoculated into meat tubes yielded a pure culture of *Bact. funduliformis*. The organisms were extremely pleomorphic, forming filaments and large bodies and exhibiting L-type variation. This strain, designated as No. 132, has been extensively studied.[8-11]

BACTERIOLOGIC OBSERVATIONS

A great many species names have been given to the numerous strains of Bacteroides isolated in the last fifty years. The classification proposed by Weinberg et al.[5] affords an instructive outline of the situation. The more recent classification of Prévot[41] appears to possess certain fundamental merit in its broader aspects, but much more study is needed before any conclusion can be reached concerning which strains are true species and which are merely varieties.

Substantial progress has been made in Rettger's laboratory, where seventy-three strains of Bacteroides were found to fall into four serologic groups.[35] Later, two groups were recognized, chiefly on the basis of whether the strains were pleomorphic or nonpleomorphic.[42] Henthorne, Thompson and Beaver[25] found that six pleomorphic strains fell into one serologic group, whereas three nonpleomorphic strains fell into another. We have adopted the convention of placing pleomorphic strains in a *Bact. funduliformis* group and nonpleomorphic strains in a *Bact. fragilis* group. The latter corresponds to the *Bact. vulgatus* group of Lewis and Rettger.[42] The name "*fragilis*" is preferred because of its general use in the literature dealing with strains from infectious processes. This simple separation into two groups is obviously a temporary expedient, but it seems to have some clinical merit, since the septicemias due to pleomorphic strains appear to be severer than those due to nonpleomorphic strains.

Following is a résumé of data on strains recovered in this laboratory.

Meat tubes sealed with paraffin and Brewer's thioglycollate broth[43] proved to be satisfactory liquid mediums. For primary isolation, these mediums are enriched with 30 per cent ascitic fluid, to obtain growth within twenty-four to forty-eight hours. In an unenriched medium, growth may not appear until after a week or more.

Both pleomorphic and nonpleomorphic strains grow diffusely, with occasional exceptions in each group. Pleomorphic strains produce large, round bodies in abundance and often chains and filaments. Gas production is vigorous, and the cultures have a foul smell. Nonpleomorphic strains grow as uniform, small bacilli, produce less gas and have a less marked odor.

Anaerobiosis for plate cultures was obtained by the Fortner method.[11] After forty-eight hours' incubation, colonies on ascitic agar plates average 1 mm. in diameter. On blood-agar plates they are smaller. The colonies are smooth, white or gray, convex with an entire edge and nonhemolytic. Some pleomorphic strains produce yellow colonies and may exhibit beta hemolysis inconstantly. Of seven pleomorphic strains, three produced pleuropneumonia-like colonies as variant growth forms (L-type variation). Both L-type colonies and regular bacilli were seen to develop from the large bodies, which are so frequent in these strains and which were shown to contain a nuclear apparatus.[9 11]

Of three pleomorphic strains tested, all produced hydrogen sulfide and one produced indol. Of four nonpleomorphic strains tested, two produced small amounts of hydrogen sulfide and none produced indol. Heat-resistance tests made with three pleomorphic and two nonpleomorphic strains showed that the organisms did not survive a temperature of 60°C. for twenty minutes. A nonpleomorphic strain from a case of meningitis produced large capsules. Motile organisms were never seen, nor were spores. The large bodies cannot be regarded as spores, since they are not heat-resistant and do not have the highly refractile quality characteristic of spores. All strains were gram-negative and strictly anaerobic.

Cultures of three pleomorphic strains injected subcutaneously into guinea pigs and rabbits produced only local abscesses. Intravenous injection of rabbits occasionally resulted in death with multiple abscesses or accompanied by cachexia with no localized lesions. Mice two weeks old injected intraperitoneally with one strain died within forty-eight hours with diffuse peritonitis. Old mice were not susceptible.

DISCUSSION

Bacteroides are natural inhabitants of mucous membranes, from which sites they may invade the tissues, blood or body cavities. They give rise to, or participate in, a great variety of pathologic processes. That Bacteroides infections are by no means rare is attested by the observation of 20 cases in this hospital within four years. The types of infection can be classified as follows: septicemia arising from throat infections, otitis media, surgery or infections of the large bowel, surgery or infections of the genitourinary tract or gunshot wounds; meningitis arising from chronic otitis media; peritonitis arising from appendicitis or leakage from colon (a mixed infection) or from salpingitis; infections of mucous membranes, including tonsillitis, otitis media, chronic cervicitis, and chronic prostatitis; and abscesses of the tonsils, liver, lungs, joints, brain, kidneys, Bartholin's glands, periurethral glands and skin.

The most frequent severe Bacteroides infections are septicemias arising from throat infections or following operations on the large bowel and meningitides arising from chronic otitis media. A case of Bacteroides peritonitis arising from salpingitis

and clinically simulating gonococcal peritonitis is noteworthy. The occurrence of Bacteroides septicemias in epidemic form in a group of soldiers with gunshot wounds, as described by Bogdán,[26] is of unusual interest. Although most Bacteroides infections appear to arise from organisms that are part of the normal body flora, this epidemic suggests that in some cases implantation of particularly virulent strains is a factor, and indicates the desirability of isolating recognized cases occurring in hospitals containing wounded men.

It is curious that Bacteroides and infections produced by them are not mentioned in some outstanding clinical and bacteriologic textbooks. This neglect is probably due to the fact that these organisms are easily missed in routine bacteriologic study, since they are anaerobic, tend to grow slowly and often require the presence of serum or ascitic fluid in the medium. It is hoped that this paper will stimulate more careful search for these organisms.

Summary

A review of Bacteroides infections based on cases collected from the literature and on those seen at the Massachusetts General Hospital is presented. The types of infections in which Bacteroides should be suspected are described. Methods for the cultivation and classification of the organisms are discussed.

Treatment consists chiefly of surgical and supportive measures. Animal experiments indicate that sulfonamides may be of value, but there is as yet no conclusive clinical evidence to this effect.

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ALKALOSIS DURING SULFADIAZINE THERAPY FOR PNEUMOCOCCAL MENINGITIS*

Report of a Case

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MENINGITIS due to a pneumococcus has a high mortality.[1] When complicated by diabetes and poor kidney function, it becomes a problem in therapy, as illustrated by the following case.

A 61-year-old, Italian housewife entered the Rhode Island Hospital on March 13, 1944, in a comatose state with a 4-day history of headache, backache, epigastric pain and vomiting. She had become drowsy 12 hours before admission and had gradually lapsed into coma.

Physical examination revealed a comatose woman breathing noisily and heavily through the mouth. The skin was clear. The eyes deviated to the left. The pupils were equal. The ears were normal. The neck was rigid. The lungs, heart and abdomen were not remarkable. The blood pressure was 180/90. The temperature by mouth was 104.2°F. The extremities showed no edema or varicosities. Bilateral Kernig signs were elicited. The patella and biceps reflexes were normal.

On admission the patient was suspected of having meningitis. A lumbar puncture yielded cloudy fluid under 370 mm. of pressure containing Type 3 pneumococci. The blood-sugar level was 680 mg. per 100 cc. and the carbon dioxide combining power 33 vols. per cent. The blood urea nitrogen was 26 mg. per 100 cc., and the creatinine 3.2 mg. The blood culture developed Type 3 pneumococcus. A blood Hinton reaction was positive. The urine showed a ++++ test for sugar, a ++ test for albumin, a specific gravity of 1.022 and a positive test for acetone. The sediment contained many red and white cells and numerous granular casts. The white-cell count was 27,800, with 93 per cent polymorphonuclear leukocytes and 7 per cent lymphocytes. The red-cell count was 3,900,000, and the hemoglobin 13.1 gm.

Within the first 2 hours of admission, the patient was started on 5 gm. of sulfadiazine intravenously and was given 100,000 units of Type 3 antipneumococcus serum by the same route (Fig. 1). She was given 50 units of regular insulin and 50 units of protamine-zinc insulin subcutaneously and also 50 units of regular insulin in normal saline solution parenterally. Twelve hours later, she was started on a pre-coma regime consisting of 5 units of regular insulin for each "+" of sugar in the urine. She received 2 gm. of sulfadiazine intravenously every 8 hours. The total parenteral fluid therapy during the first day totaled 2000 cc. of normal saline solution and 2000 cc. of 5 per cent dextrose solution. The patient was still in coma the following day. The urinary output was extremely low. The sediment continued to show many red and white cells and a ++ test for albumin. The blood-sugar level had dropped to 362 mg. per 100 cc. Fifty thousand more units of antiserum was given.

On the 3rd hospital day, the patient responded to treatment and began to take sodium bicarbonate (1 heaping teaspoonful in water every 2 hours, alternating with and without sulfadiazine). The blood culture was sterile. X-ray films of the chest showed no abnormalities. The blood urea nitrogen had risen to 41 mg. per 100 cc., and the creatinine to 3.3 mg. The blood-sulfadiazine level was 18.8 mg. per 100 cc. of free drug and 22.6 mg. of total drug. The urinary sediment still contained numerous red and white cells and albumin.

On the 4th day, the blood urea nitrogen was 54 mg. per 100 cc., and the blood-sulfadiazine level 20.2 mg. of free and 28.6 mg. of total drug. On the 5th day, the temperature was almost normal, and the patient was subjectively and objectively much better. The blood urea nitrogen was 56 mg. per 100 cc., the creatinine 5 mg., and the sugar 414 mg. Sodium bicarbonate was continued as previously noted. On the 6th day, diarrhea and distention were noted. Sodium bicarbonate was given only once every 4 hours. Kaopectate and paregoric were administered. On the 7th day, the patient was well enough to take a liquid diet. She was still receiving parenteral fluids. On the following day, however, she became less responsive and had a convulsive seizure. The eyes deviated to the left, and there was spasm of the right side of the face and spasticity of the entire body. After the seizure, twitching of various muscles of the body was noted, particularly those of the face and upper extremities.

From the 3rd to the 8th day, the patient received 345 gm. of sodium bicarbonate by mouth. The total fluid intake by all routes in this period amounted to 17,600 cc., and the total urinary output was 5020 cc.

On the 8th day, the carbon dioxide combining power was 110 vols. per cent, compared with 33 vols. 7 days previously. The whole-blood chloride level, expressed as sodium chloride, was 292 mg. per 100 cc., and the blood-sulfadiazine level 14.2 mg. of free and 25.1 mg. of total drug. The Chvostek sign was markedly positive, and the patient was having periods of apnea, followed by rapid breathing. She was stuporous, but responded to vigorous shaking and took fluids by mouth. She was given calcium chloride by vein and ammonium chloride by mouth. The convulsive seizures stopped, but the twitching of various muscles continued. An attempt was made to increase the chlorides by intravenous normal saline solution, since the patient had improved only slightly after 24 hours' treatment with 18.5 gm. of ammonium chloride and 3 gm. of calcium chloride. Breathing of 10 per cent carbon dioxide and 90 per cent oxygen was attempted to relieve the apneic phases, but this had only a temporary effect. Ten cubic centimeters of 0.07 per cent hydrochloric acid and 5 cc. of 0.5 per cent hydrochloric acid were administered intravenously, but no more was given for fear of further damaging the kidneys by formation of acid hematin. The patient was becoming edematous. Abdominal distention due to gas was marked.

In one day the carbon dioxide combining power was brought down to only 104 vols. per cent. The sodium chloride had risen to 330 mg., the blood urea nitrogen was 50 mg. per 100 cc., and the creatinine 5.1 mg.

On the 10th day, after one more day of treatment of the alkalosis with 2 gm. of calcium chloride intravenously and 6 gm. of ammonium chloride by mouth, the carbon dioxide combining power was down to 86 vols. per cent and the sodium chloride up to 378 mg. The blood urea nitrogen was 50 mg., and the creatinine 6 mg. per 100 cc. The patient looked much better, but the urinary output was decreasing.

On the 11th day, because the kidney output was only 400 cc., ureteral catheterization was done. Sulfadiazine was stopped because the patient had run a near-normal temperature for several days and because it was suspected that kidney shutdown might have been due to the drug. Insulin was also stopped, because with the decrease in infection the severity of the diabetes decreased. The blood urea nitrogen had risen to 62 mg. and the creatinine to 6.5 mg.; the carbon dioxide combining power had dropped to 75 vols. per cent, and the sodium chloride to 332 mg.

On the 12th day, the kidney output was less than 100 cc. Tissue edema was marked. The urine was small in amount and was grossly bloody and full of sediment.

On the 15th day, after persistent continued treatment with intravenous solutions, the kidneys were excreting large amounts of urine. Because the total protein was 3.7 gm. per 100 cc., 500 cc. of blood plasma was given in an attempt to relieve the edema. The creatinine was 8.8 mg., the blood urea nitrogen 96 mg., and the sodium chloride 340 mg. per 100 cc. On the 17th day, the urinary output continued high. Edema had decreased considerably. The patient felt well and was put on a liquid diet. A lumbar puncture yielded spinal fluid with an initial pressure of 350 mm., a protein of

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28 mg. per 100 cc. and 1 polymorphonuclear and 10 lymphocytic cells per cubic millimeter. The blood urea nitrogen and creatinine levels were dropping, and the carbon dioxide combining power was 62 vols. per cent. Two days later the patient became comatose. No cause was found, although cerebral thrombosis was suspected. She came out of coma without treatment in 6 hours.

On the 24th day, the patient developed a temperature of 103.5°F. Lobar pneumonia was diagnosed clinically. X-ray examination showed consolidation in the chest. A lumbar puncture yielded clear spinal fluid with 95 mg. of protein per 100 cc., 45 polymorphonuclear cells and 25 lymphocytes per cubic millimeter, a positive Hinton reaction and a gold-sol curve of 5554321000.

On the 26th day, blood and urine cultures were reported as positive for a coagulase-positive *Staphylococcus aureus*. The blood urea nitrogen was 48 mg., the creatinine 3.3 mg., and the blood sugar 268 mg. The white-cell count was 12,700.

The patient was started on penicillin, being given 15,000 units intramuscularly every 3 hours. The response both clinically and subjectively was excellent. The temperature dropped to normal. In 3 days she received 195,000 Oxford units of penicillin, and recovery from the pneumonia and septicemia appeared probable when the patient suddenly had a convulsive seizure lasting 5 minutes and died.

Permission for autopsy was refused.

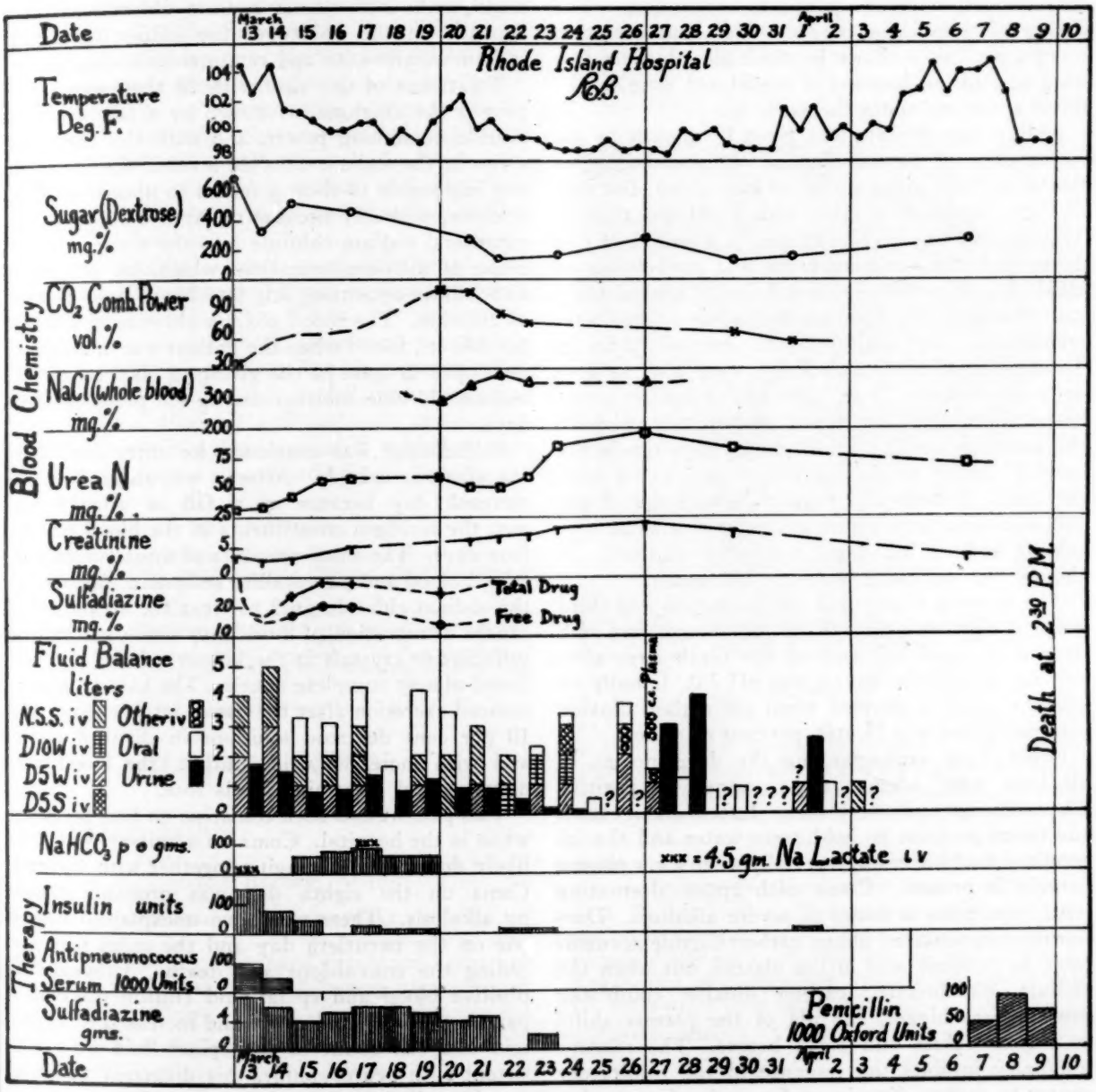

FIGURE 1.

DISCUSSION

On admission, the carbon dioxide combining power of 33 vols. per cent and a positive test for acetone in the urine indicated that diabetes mellitus was a contributing, but not the major, factor in producing unconsciousness. The need for insulin, in

this previously unknown diabetic patient, decreased as the infection was controlled. She had poor kidney function, as shown by the urine sediment and albumin, a specific gravity of 1.022 in the presence of both albumin and sugar, and nitrogen retention that increased after adequate hydration. The dosage of sulfadiazine was not high, but excretion was poor. This is shown by the high values for free drug and by an amount of acetylated drug in the blood about ten times the usual one.

Sodium bicarbonate was given by mouth to aid in excretion of the sulfadiazine. In pneumonia patients we have given up to 60 gm. a day, but still find in some cases a urine with a pH less than 7. This patient was given 345 gm. in a period of five days, with the resulting coma and convulsions of alkalosis. The kidney insufficiency undoubtedly contributed to the alkalosis by failure of acid-base regulation. In subjects with normal kidneys, Thompson, Mitchell and Kolb[2] were able to give daily doses of 60, 75 and 130 gm. of sodium bicarbonate in a three-day period, respectively, without the development of alkalosis and with a rise in the carbon dioxide combining power only to 68 vols. per cent. Jeghers and Lerner[3] believe that 8 per cent of cases of peptic ulcer treated with alkalies containing sodium bicarbonate develop alkalosis, although the syndrome is seldom recognized.

The reaction of the urine on the second and third hospital days was pH 5.0. On the fourth and fifth days it was pH 8.0, and on the ninth day, after one day of acid therapy, it was pH 7.0. Usually an alkaline urine is excreted when the carbon dioxide combining power is 75 vols. per cent or more.

Other signs accompanying the development of alkalosis were edema, coma, apnea, a positive Chvostek sign and convulsions. Excess alkali causes the tissue proteins to hold more water and the interstitial fluid increases, especially when a low plasma protein is present. Coma with apnea alternating with hyperpnea is found in severe alkalosis. During the compensated phase, carbon dioxide accumulates as carbonic acid in the plasma, but when the sodium bicarbonate (carbon dioxide combining power) rises higher, the pH of the plasma shifts to higher values and coma begins. The relative alkalinity inhibits the response of the respiratory center to carbon dioxide, and periods of apnea followed by deep respiration may result. It also decreases the ionization of calcium compounds in the plasma, although there is no decrease in total calcium. With less than normal calcium ions neuromuscular irritability is increased, so that the Chvostek sign is positive, and with marked changes, convulsions may begin.

Calcium chloride is useful for emergency treatment, since for an hour or two it supplies extra calcium ions, and it also has a slight acidification action. Ammonium chloride is a better agent, since the cation is converted to urea by the liver and some bicarbonate is replaced by chloride. The giving of intravenous hydrochloric acid is a rather direct attack on the alkalosis, since its reaction with bicarbonate forms carbon dioxide, which is excreted by the lungs, and sodium chloride. Treatment with intravenous sodium chloride solution depends on the ability of the kidney to excrete sodium bicarbonate and retain sodium chloride.

Treatment of this case with all these agents improved the alkalosis, as shown by a fall in carbon dioxide combining power, and with this there was a rise in the sodium chloride level of the blood. It was impossible to show a return to normal of blood chloride, probably because of rapid diffusion of the parenteral sodium chloride into the tissues and because of nitrogen retention, which, by phosphate and sulfate retention, left less blood base to exist as chloride. The blood sodium chloride of 292 mg. per 100 cc., found when the patient was in alkalosis, developed in spite of the giving of 9000 cc. of 0.85 sodium chloride solution during the previous seven days.

Sulfadiazine was continued for three days after the alkalosis episode. After it was stopped on the eleventh day because of a fall in urinary output, the nitrogen constituents of the blood rose for four days. The small amounts of urine voided contained blood and a crystalline sediment. Apparently the sodium chloride used to treat the alkalosis had caused a migration of fluids into tissue spaces, and sulfadiazine crystals in the kidney tubules had produced almost complete anuria. The kidneys recommenced excretion after the use of intravenous 5 and 10 per cent dextrose solutions in distilled water, and with increased urine output, the blood urea nitrogen and creatinine levels rose.

This patient had been comatose on four occasions while in the hospital. Coma on admission was most likely due to the meningitis together with diabetes. Coma on the eighth day was probably caused by alkalosis. There were two unexplained comas, one on the twentieth day and the other just preceding the convulsions and death. Although the positive blood and spinal-fluid Hinton reaction, a paretic colloidal-gold curve and increased total protein and cell count of the spinal fluid were consistent with neurosyphilis, this diagnosis was relegated to the background owing to the severer and more obvious infections present during the illness. It is unlikely that meningovascular syphilis was a contributing factor in this patient's death. Localized abscesses are found complicating pneumococcal meningitis. That this was the cause of death is not so likely. There were no progressive symptoms indicating increase in intracranial pressure, nor was the initial pressure on the last tap elevated. Other possible causes of death are a cerebral hemorrhage on a hypertensive basis, acute staphylococcal endocarditis with ruptured aortic cusp and resulting lodgment of an embolus in the cerebral artery, and an acute myocardial failure from the severe

and long illness. The last seems the most probable cause.

Conclusions

The administration of sulfadiazine and specific antipneumococcus serum helps to sterilize the blood stream and spinal fluid in cases of Type 3 infection.

A damaged kidney not only excretes sulfadiazine poorly but may cause alkalosis if sodium bicarbonate is given in considerable dosage with the sulfonamide. Careful observations of the blood urea nitrogen and blood-sulfonamide levels, the carbon dioxide combining power and the fluid balance are necessary in cases in which kidney function is abnormal.

Treatment of an alkalosis may cause renal shutdown when large amounts of sulfadiazine are present in the body.

Apparent sterilization of blood and spinal fluid from Type 3 pneumococci with specific antipneumococcus serum and sulfadiazine, apparent recovery from alkalosis and apparent sterilization of blood from *Staph. aureus* with penicillin were insufficient to save this patient's life.

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CLINICAL NOTE

CUTANEOUS HORN

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PATIENTS with pronounced cutaneous horns are so rarely seen that the following case appears worthy of recording.

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An 88-year-old man was admitted to the New Hampshire State Hospital with a horny growth on the back of the right hand (Fig. 1). It was about 15 cm. long, curving distally in a semicircle from the area of origin over the first and second metacarpophalangeal joints to the middle phalanx of the ring finger. It was apparently a hyperkeratosis. A relative stated that the growth started as a wart 10 years previously, and that the patient used to trim it with a razor blade. Gradually the tissue became hard and he filed or ground it down.

The growth was removed in toto and sent to the pathologist. According to the report, the specimen consisted of a

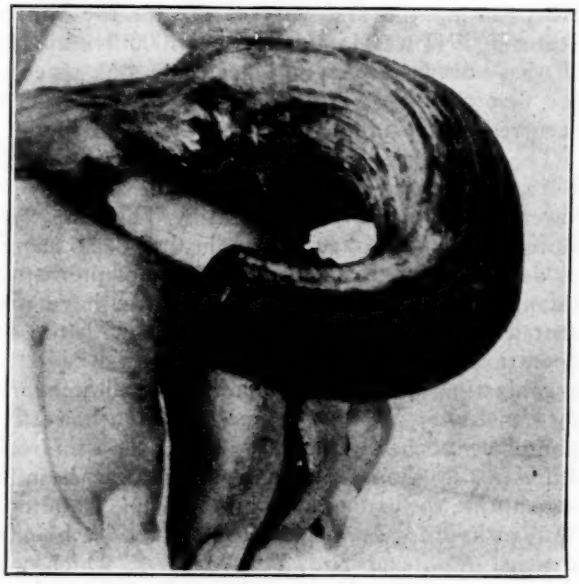

Figure 1.

horn 14.5 cm. long in the shape of the letter C. The diameter at the base was 4 cm., and that at the tip, which was blunt, was 1.3 cm. The horn was longitudinally striated. The color varied from light brown at the proximal end to dark brown at the tip. Microscopic examination of the tissue at the base revealed stratified squamous epithelium with long papillary processes, overlying fibrous connective tissue in which there were many lymphocytes. The stratum corneum was composed of innumerable layers. There was no evidence of malignant degeneration. The diagnosis was cutaneous horn.

The patient made an uneventful recovery from a skin graft, and is still in the hospital.

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MEDICAL PROGRESS

DISEASES OF THE NEWBORN*

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THE relatively high death rates that still prevail during early infancy are the cause of much concern throughout the country. The infant mortality during the first year of life for the United States in 1941 was 45.3 deaths per 1000 live births.[1] Of these deaths 27.7, or 61 per cent, took place in the first month of life, while 18.1 or 29 per cent occurred in the first twenty-four hours of life.[2,3]

The federal government, through the Children's Bureau, has taken a leading role in attempts to lower the incidence of such deaths. The Children's Bureau has encouraged state health departments to develop plans to improve the care of premature infants, and at least forty-three states have presented such a program.[4] The Bureau, with the cooperation of various nationally recognized pediatric organizations, has prepared and published *Standards for the Care of Newborn Infants*. This authoritative pamphlet can be obtained by writing the Children's Bureau and should be studied by every hospital attempting the care of such infants. The Children's Bureau has also developed and published a booklet entitled *Plans for Hospital Nurseries*, which was drawn up with a view to protect the infants from infection and to facilitate the work of physicians and nurses.[4] In addition, as a wartime measure, the Bureau has been given the responsibility of administrating the Emergency Maternal and Infant Care (EMIC) Program for the wives and infants of enlisted men.

PREMATURITY

The ideal method of decreasing the number of deaths from prematurity would be to prevent the premature onset of labor; up to the present time, however, no one has succeeded in doing this except in a few isolated cases. It is therefore necessary to improve the environment into which the premature infant is born if its chances of survival are to be increased.[5]

Although a premature infant may suffer and die from any of the pathologic conditions affecting an infant born at term, there are many who fail to show pathologic lesions that can be discovered by known chemical or histologic means. The immediate reason why the majority of otherwise normal premature infants die is inability to absorb oxygen through the inadequately developed lung. As the fetus grows, capillaries gradually branch out from the septal vessels and push their way between the cuboidal alveolar cells, thrusting them aside so the capillaries lie uncovered in direct contact with the air spaces. If the capillaries in contact with the air and capable of receiving oxygen are too small to support life, the infant cannot survive. An effective method of oxygen therapy increases the percentage of oxygen in the inspired air and thus allows greater absorption.[5] Many small premature infants have survived in an atmosphere containing 50 per cent oxygen for several months or until they have developed sufficiently to live under normal atmospheric conditions.[6]

Stevenson has made an important clinical application of the use of carbonic anhydrase in disease of the newborn.[7] The action of this biologic catalyst is to expedite the liberation of carbon dioxide from carbonic acid. Without its influence this gas cannot be unloaded from the blood at a speed commensurate with the rate of pulmonary circulation. This delay indirectly impedes the uptake of oxygen, for which reason oxygen therapy is of no avail. Stevenson found that the concentration of circulating carbonic anhydrase is low in the newborn, and even lower in the premature infant. It is likely to be especially low in such infants as are cyanotic without obvious reason. The mortality rate in these cases is high, but post-mortem examination reveals little cause of death. Certainly, the older notion of congenital atelectasis is fallacious in such cases. When, however, these infants are transfused, their blood enzymes become rapidly elevated and their cyanosis disappears; furthermore, the mortality rate is considerably lowered.

Feeding and energy requirements. Gordon[8] states that the caloric intake of premature infants during the first few days of life is a matter of no real concern. Even though the caloric intake is zero the total negative energy balance is small since the basal metabolism is only 40 to 50 calories per kilogram per day and the quotas for fecal loss and specific dynamic action, which depends on the food intake, are small. For older premature infants the basal metabolic rate in terms of body weight averaged 58 calories per kilogram per day. The only change in the number of calories per kilogram from week to week was an increase of 5.3 calories from the first to the second week of postnatal life.[9]

The total caloric requirement of premature infants is from 75 to 90 calories per kilogram per day for the first two or three weeks of life, and thereafter 100 to 125 calories.[10,11]

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The premature infants have the power to metabolize carbohydrate as efficiently as do full-term infants.[9] They also have an ability to absorb protein equal to that observed in full-term infants.[11] Many premature infants exhibit a defect in their alimentary absorption of fat, irrespective of the type of fat, but inability of the alimentary tract to split fat is not the determining factor in this defective absorption. Whether the defect in the transport of fat across the intestinal wall is dependent on an anatomic underdevelopment of the capillaries and villi, or a functional impairment of the enzyme mechanisms concerned with phosphorylation of fat or on differences of intestinal motility is a problem reserved for future study. Whatever the mechanism involved, Levine and Gordon[12] are convinced that the failure of some premature infants to thrive on presumably adequate diets may be the result of faulty absorption of ingested fat. These authors recommend a reduced fat content in the diet for premature infants and the maintenance of the total dietary calories at the same level by replacement with protein and carbohydrate. Their feeding mixture contains 120 calories per kilogram of body weight, and the total fluid volume is 150 cc. per kilogram, the basic constituents being 2.5 gm. of fat, 18 gm. of carbohydrate and 6 gm. of protein per kilogram.

Levine and Gordon[11] question the assumption that human milk is the ideal food for premature infants. They point out that it is a relatively dilute feeding and it may predispose to increased peristalsis and diarrhea, abdominal distention and respiratory embarrassment. It is relatively high in fat. It is low in mineral content, particularly in calcium and phosphorus, and there is abundant evidence to prove that, even though all the calcium and phosphorus contained in the daily amounts of human milk ordinarily ingested by the premature infant are completely absorbed and utilized, the amounts are still insufficient to meet the demands for bone growth during the first year, as determined by chemical analysis of the bones of fetuses and by studies of mineral retention.[13] Human milk is relatively low in protein, and it has been shown that augmentation of the protein intake is accompanied by an increased alimentary absorption of the protein ingested. The rapid rate of body growth of premature infants implies the desirability of a correspondingly high protein intake for the manufacture of the needed extra protoplasm.

There are certain arguments in favor of human milk as the ideal food for premature infants. Teleologically, a food supplied by nature is preferable to any form of artificial food. There is suggestive, but not conclusive, evidence that immune substances may be transferred in the breast milk and particularly in the colostrum. Nursing at the breast has many practical and economic advantages. The physiologic and psychologic benefits to the mother of suckling her infant at the breast cannot be gainsaid. Finally, human milk has a low content of electrolytes and the renal excretion of such substances may be better handled in this form by the premature infant, whose kidneys have been shown to be less efficient excretory organs than those of full-term infants.[11]

Regarding the relative merits of human and cow's milk as the ideal food for premature infants Levine and Gordon[11] suggest that in hospital practice or when human milk is not available except at great expense a cow's milk mixture low in fat is an adequate substitute.

Fluid requirements. Levine and Gordon[11] recommend the routine use of relatively low fluid intakes —130 to 150 cc. per kilogram of body weight — in the feeding of premature infants. When fluid intake was below 95 cc. per kilogram large amounts of water were withdrawn from the body, resulting in a negative water balance and dehydration. With higher fluid intakes the infants retained in their bodies a relatively fixed amount and merely eliminated the extra water as extra urine.

Vitamins. The tendency of the premature infant to have hemorrhagic manifestations of a serious nature is explained by the fragility of his capillaries and the low prothrombin content of his blood plasma. The paucity of vascular elastic tissue, the frequent occurrence of anoxia with its deleterious effect on capillary integrity and the low body reserves of vitamin C required for building so-called "cementing substances" are probably the chief factors contributing to the increased permeability of the capillaries of the premature infant.

Levine, Marples and Gordon[14] have recently demonstrated the important role of vitamin C in the intermediary metabolism of protein in premature infants. The action of vitamin C is specific in completing the oxidation of two aromatic amino acids, phenylalamine and tyrosine. A defect in aromatic-amino acid metabolism can be produced at will in premature infants by feeding mixtures of cows' milk containing 5 gm. or more of milk protein per kilogram of body weight and by withholding vitamin C. The defect can be promptly eradicated by the administration of vitamin C in adequate dosage. The authors therefore recommend that all premature infants be given 25 to 50 mg. of ascorbic acid daily from birth and from 75 to 100 mg. daily after feedings of cows' milk have been instituted.

A reduced antenatal storage of calcium, phosphorus and possibly vitamin D predisposes the premature infant to rickets. Added to this predisposition is the defect in fat absorption and presumably in the fat-soluble vitamins, as well as the rapid rate of body growth and the increased demands for retention of calcium and phosphorus, often in the face of a diminished dietary supply provided in human milk. Even if vitamin D is administered and absorbed in adequate amounts, its efficacy in

promoting renal tubular reabsorption of phosphate, which Harrison[15] has demonstrated to be one of the functions of this vitamin in older subjects, may be minimal as a result of the defect in renal function. This impairment, together with faulty alimentary absorption of vitamin D, may explain the high dosage of the vitamin needed to prevent rickets in premature infants.

Miscellaneous Congenital Defects

Warkany[16] has submitted further proof to defend his thesis that certain types of maternal nutritional deficiency can result in specific malformations in the young. The offspring of female rats reared and bred on a diet deficient in the vitamin factor found in pigs' liver produced 32 per cent abnormal offspring. The addition of 2 per cent dried pig liver to the diet prior to the fourteenth day after mating prevented the occurrence of deformities. The defects occurred in the skeletal system and included shortness of the mandible, shortness or absence of the radius, ulna, tibia or fibula and fusion of the ribs and of the sternal centers of ossification. In another experiment Warkany[17] observed congenital skeletal malformations in 45 per cent of the offspring of female rats fed a rachitogenic diet. The changes observed comprised a pronounced curving of the radius, ulna, tibia and fibula, as well as angulation of the ribs, and were quite distinct from those seen in the vitamin B deficient diet. The addition of vitamin D to the maternal diet prevented these malformations. In his most recent communication Warkany[18] describes marked maldevelopment of the eye in the offspring of female rats fed a diet deficient in vitamin A.

New light has recently been thrown on the etiologic factors involved in certain congenital malformations by three series of cases reported from Australia in which virus infections, particularly German measles, occurring early in pregnancy seem to be definitely related to congenital defects.[19] Gregg reported a series of 78 patients with congenital cataract, 44 of whom also had congenital heart disease, occurring in infants whose mothers, with few exceptions, had suffered from what was presumed to be German measles in the early months of pregnancy. Swan reported 49 cases of rubella occurring in all stages of pregnancy, of which 25 occurred in the first two months, every one of which showed congenital defects, usually of the eye or heart. In 50 per cent of those having rubella in the third month the infants showed defects. The congenital malformations encountered were 17 heart lesions, 14 defects of the eye, 7 deaf mutes, 1 mongoloid idiot and several cases each of microcephaly, hypospadias and mental retardation. In a follow-up communication Swan added 10 more cases of congenital malformations occurring in infants born of mothers who had had rubella early in pregnancy. Reese reported 3 cases. Erickson[19] added 11 cases of congenital cataract and congenital heart disease occurring under similar conditions in this country.

Both Swan and Erickson raise the question whether therapeutic abortion is justified if rubella occurs during the first two months of pregnancy, since in the experience of both, 100 per cent of such babies had serious congenital malformations.

Esophageal Atresia and Tracheoesophageal Fistulas

Esophageal atresia and tracheoesophageal fistulas have formerly been considered incompatible with life. In the last few years, however, a few successes or partial successes have been reported from various parts of the country and it now appears correct that surgical intervention should be attempted. Ladd[20] has recently reported 39 such patients operated on at the Children's Hospital, of whom 11 are living. He emphasizes that the surgical approach to combat this condition is subject to change but that, at the present time, primary anastomosis of the esophagus is the operation of choice when the two ends of the esophagus can be approximated without too much tension. In cases in which the ends of the eosphagus are far apart, the three-stage operation, with the ultimate construction of an anterior thoracic esophagus, is a safer operation. The last 5 patients operated on according to this plan are living and doing well.

Ladd predicts that, if obstetricians and pediatricians are alert and make an early diagnosis, the mortality will be further lowered.

The diagnosis may be suspected when the newborn infant has an excess of mucus or saliva in the mouth, with or without an associated cyanosis. The next suggestive symptom is vomiting of mucus even though no food or fluid has been given, or vomiting after the first feeding. It is essential to a good prognosis, however, that the diagnosis be made before food is given, since its presence in the lung will probably result in a pneumonia. On the least suspicion, a stiff catheter should be passed down the esophagus in order to demonstrate a blind pouch. If in doubt x-ray films should be taken with the catheter in place. Barium should not be given, since its presence in the lung results in an inflammatory reaction; if an opaque medium is needed it is much safer to use lipiodol. The presence or absence of rales in the lungs and of air in the intestinal tract depends on the type of anomaly present.

Spina Bifida and Cranium Bifidum

Ingraham and Swan[21] have analyzed 546 infants and children seen at the Children's Hospital during the last twenty years to see whether there can be established any reasonably definite criteria for prognosis, for operative therapy and for operative technics. They also wished to discover if the general attitude of hopeless pessimism toward these cases should not be modified by examination of the end

results. The authors found that 30 per cent of the patients with spina bifida and 34 per cent of those with encephalocele may expect a relatively normal life. They concluded that an unduly pessimistic prognosis is unwarranted until individual evaluation has been carefully pursued.

Ingraham and Scott[22] have also presented a series of 20 cases with the Arnold–Chiari malformation to emphasize that this is not a rare condition but is a frequent accompaniment of myelomeningocele. This malformation is a congenital anomaly of the hind brain characterized by a downward elongation of the cerebellum and brain stem into the cervical portion of the bony spinal canal. Surgical treatment should be limited to patients without extensive paralysis of the lower extremities and sphincters. It should not be offered if hydrocephalus is so advanced that it is inconsistent with normal mental development. The authors believe that encephalography may help in identifying the associated microgyria, which is probably another contraindication to operation.

Congenital Cerebral Palsy

Until twenty-five years ago Little's disease or congenital cerebral palsy was held to be the result of various factors, chiefly birth trauma, acting during birth on the central nervous system. Of late, doubt concerning the prime etiologic role of birth trauma has arisen because of post-mortem examinations that failed to show any evidence of birth trauma and because there was a high incidence of essentially normal birth histories in these cases. Yannet[23] analyzed 86 patients in whom the diagnosis of congenital cerebral palsy had been made and uncovered data showing the major importance of developmental cerebral defects in the etiology, as well as information on certain genetic relations. Yannet found the average age of the mothers at the time of birth of the affected child was significantly greater than that of child-bearing women in the general population. The affected children tended to have a later ordinal birth rank than would be normally expected. There was a significant incidence of similarly affected siblings of patients with cerebral palsy. The incidence of mental deficiency in the nonaffected siblings was greater than would be expected from random selection. Finally, there was an unusually high incidence of associated physical defects, especially those involving the eyes.

Erythroblastosis Fetalis

The pathogenesis of erythroblastosis fetalis has been established in great measure through the brilliant work of Philip Levine, who has recently published an excellent review of the subject.[24] Erythroblastosis fetalis is caused by isoimmunization of the mother by a dominant hereditary blood factor in the fetus, most frequently the Rh (rhesus) factor. This intrauterine hemolytic disease of the fetus and the newborn infant occurs under highly specific conditions, determined by the presence or absence of the Rh factor in the parents. In more than 90 per cent of the cases the father's blood contains the Rh factor (Rh+), the mother's blood lacks the factor (Rh—) and the fetal blood possesses it (Rh+). The two essential steps in the pathogenesis of erythroblastosis fetalis are the response of the Rh— mother to the Rh+ fetal blood by production of anti-Rh agglutinins and the continuous passage of maternal anti-Rh agglutinins through the placenta to react with and hemolyze the susceptible fetal Rh+ blood.

In 1940, Landsteiner and Wiener studied the specificity of an immune serum produced in rabbits and guinea pigs by injections of the blood of *Macacus rhesus*. This serum was found to agglutinate 85 per cent of all human bloods. These bloods were termed Rh+, and the 15 per cent inactive bloods, Rh—. The experimental anti-Rh serum produced by rabbits or guinea pigs cannot as yet be used as a routine diagnostic serum, since the resulting agglutinations are unreliable or difficult to read. For Rh typing one has had to depend, until recently, on high-titer human serum, which is found in only about 1 of 20 mothers of erythroblastotic infants. Since the Rh factor is a mosaic composed of several antigenic substances, not all the human anti-Rh serums in contrast to anti-A or anti-B testing serums, give parallel reactions.[24] There are, as a result, three main types of human anti-Rh serums: that agglutinating 87 per cent of random bloods and called "anti-Rh′" by Wiener and Landsteiner; that agglutinating 85 per cent of random bloods, called "anti-Rh"; and that agglutinating 73 per cent of random bloods, called "anti-Rh_1." It is therefore possible to have a small number of cases of proved erythroblastosis fetalis in which evidence of isoimmunization (father Rh+ and mother Rh—) cannot be obtained provided that human serum of the anti-Rh_1 type is used.

The important problem of accurate Rh typing appears to be solved by the timely work of Diamond[25] at the Children's Hospital. Working in co-operation with the Department of Physical Chemistry of Harvard Medical School, he has been able to pool and concentrate low-titer anti-Rh serums, obtaining a globulin fraction that yields accurate typing results. Furthermore, the technic of typing is simple. It consists in mixing a drop of the concentrated anti-Rh serum with a drop of the unknown red-cell suspension on a glass slide and observing at once the presence or absence of agglutination.*

*The Blood Grouping Laboratory, 300 Longwood Avenue, Boston 15, is in need of more anti-Rh typing serum for the armed forces and civilian use. Physicians and hospitals are urged to send to the laboratory a few cubic centimeters of blood from any patient known to have had a baby with erythroblastosis delivered within the last two years. If the serum is found to contain a useful amount of anti-Rh agglutinins, the physician or hospital will be notified and requested to forward from 100 to 500 cc. of the patient's blood. Seventy per cent of the concentrated serum will be set aside for the military services and 30 per cent will be available immediately to the contributing physician or hospital in the form of standard anti-Rh typing serum.

The demonstration of Rh isoimmunization is possible in 90 per cent of the mothers of erythroblastotic infants, but in 10 per cent the mothers are Rh+ and some other cause for the syndrome must be found. Levine[24] suggests that there should be other blood factors besides the Rh factor capable of inducing isoimmunization. He was able to prove this point by demonstrating atypical agglutinins produced by two Rh+ mothers of erythroblastotic infants; both serums agglutinated all Rh— bloods but did not react with other Rh+ bloods. Since this new factor had some genetic relationship to the Rh factor, Levine suggested the two letters Rh be reversed, the terms "Hr" and "anti-Hr" being used to designate this new blood factor and its corresponding antibody. The Hr factor, however, can be held responsible for isoimmunization in only some of the Rh+ mothers. In a certain number of the remaining cases, isoimmunization may perhaps be induced by the factors A or B in fetal blood. In a few cases no cause for the isoimmunization could be demonstrated by present methods. It must be remembered that in some cases a clinical syndrome indistinguishable from erythroblastosis fetalis may be the result of fetal anoxia, syphilis or septicemia.

Potter[26] insists that, to diagnose erythroblastosis anemia, erythroblastemia and splenomegaly must be present. Other manifestations usually associated are edema, jaundice, hepatomegaly and placental hypertrophy. It is important to stress these diagnostic features, since the diagnosis of erythroblastosis fetalis is being made too widely and on insufficient evidence on the one hand and is still being overlooked on the other.

In approximately 12 per cent of all marriages the wife is Rh— and the husband is Rh+. If the father is homozygot, all the offspring will be Rh+; if he is heterozygot, there is a 50 per cent chance that the infant will be Rh—. Thus, in approximately 9 per cent of all births an infant with Rh+ blood is delivered of a mother with Rh— blood, *but* erythroblastosis actually occurs in only 0.1 to 0.2 per cent of all pregnancies. The Rh typing of all pregnant women is recommended, but as a result, 120 out of every 1000 couples may be upset, even terrified, at the possibility of a forthcoming erythroblastotic infant. In all fairness the reassuring fact that this is to be expected in less than 2 per cent of such matings should be emphasized. Furthermore, even should an erythroblastotic infant be found at delivery the ultimate outlook for over half of these patients is excellent.

The pathogenesis of this disease is still far from being completely solved. The Rh factor must play an important role, but one wonders why erythroblastosis fetalis occurs in only about 2 per cent of the Rh+ infants whose mothers have Rh— blood. It is obvious that there must be other unknown factors in the equation.

The termination of pregnancy by cesarean section as soon as the fetus becomes viable has been recommended in such cases, on the assumption that if the fetus can be delivered early enough in the course of pregnancy it may escape being affected by maternal agglutinins.[26,27] It has also been suggested that the mother's blood be watched closely for the appearance of agglutinins or for a rise in agglutinin titer and that the pregnancy be terminated at the time when agglutinins appear or when the titer suddenly rises.[28] If there were no hazard associated with prematurity, early delivery might be an advisable procedure on the supposition that the more prolonged the exposure to anti-Rh agglutinins, the more severe the disease. The fetus, however, is probably affected early in pregnancy, regardless of whether demonstrable agglutinins are present in the maternal circulation; furthermore, many infants become much more severely affected immediately after delivery than they were during intrauterine life. Too few cases have as yet been reported to indicate whether early delivery with the consequent discontinuation of direct exposure to anti-Rh agglutinins can outweigh the handicap of prematurity imposed on an infant already suffering from erythroblastosis. At the Chicago Lying-in Hospital, as well as in other clinics, infants have been delivered early by cesarean section only to die of erythroblastosis despite the administration of blood at birth, and it has been concluded that nothing is to be gained by premature delivery.[26]

In the obstetric management of the mother of a potentially erythroblastic infant it is unfortunate that there is no direct connection between the presence or absence of anti-Rh agglutinins in the maternal serum and the condition of the infant. Levine[24] failed to find anti-Rh agglutinins in more than 50 per cent of the mothers, although he quotes British workers as observing a higher incidence. He states that isoimmunization may occur even in the absence of demonstrable antibodies. Neither the presence or absence of anti-Rh agglutinins nor the titer of these agglutinins is a reliable index of the presence or severity of erythroblastosis in the infant.

The treatment of erythroblastosis fetalis is by transfusion of Rh— blood from a donor other than the mother.

Infection

In spite of increased knowledge regarding causes of infection in newborn infants and methods of prevention, epidemics still occur. Reports coming to the Children's Bureau indicate that they are increasing along with overcrowding of the maternity services. In a number of hospitals in different localities epidemics of diarrhea among newborn infants have been associated with mortality rates of from 30 to 50 per cent.[2] *Standards for Care of Newborn Infants* and *Plans for Hospital Nurseries*, two booklets issued

by the Children's Bureau and previously referred to, give valuable suggestions to assist in the prevention and control of all types of infection in the newborn.

Torrey and Reese[29] have found that the initial aerobic bacterial flora of the throat and nasopharynx of artificially fed newborn infants is largely acquired through direct contact with adults and not from the parturient canal. Droplets of saliva comprise the principal vehicle of transfer. The flora in premature infants is essentially the same as that in full-term infants of similar age. Although occasional contact with adult carriers of pneumococci, influenza bacilli and beta-hemolytic streptococci occurred, the first two organisms were not present and the streptococci were only rarely present in infants from one day to four weeks old.

These authors found that up to sixteen hours after birth the nasopharynges and throats of 80 per cent of the infants exhibited sterility. Between twenty-four and forty-eight hours after birth 50 per cent of infants in wards exposed to ultraviolet irradiation still showed sterility, as contrasted with only 12 per cent of infants in wards not so exposed. Beyond that time results for the two groups were essentially alike, except in regard to hemolytic strains of *Staphylococcus aureus*. Ultraviolet irradiation did not retard the acquisition of nonhemolytic streptococci but did delay the presence of hemolytic strains of *Staph. aureus*; in the absence of ultraviolet irradiation an occasional air-borne transfer of the latter organism probably occurred.

Torrey and Reese conclude that ultraviolet irradiation does not prevent person-to-person transmission of pathogens through the air within the range of a few feet. Among infants from seven to twenty-five days old in wards without irradiation, 60 per cent were carriers of hemolytic strains of *Staph. aureus* in the nasopharynx, of which 86 per cent were coagulase positive and potential pathogens.

These workers also found that the strains of streptococci and of *Staph. aureus* normally present in the throats and nasal passages of adults passed to some extent through all types of face masks, even in the absence of coughing and sneezing. It should be pointed out, however, that they used a four-layer gauze mask in their study and not the more efficient mask with an inner layer of sheet cotton. Abramson[30] thinks that the use of the face mask in the control of droplet infection is an important integral part of preventive nursing and medical care, even though it is believed that such masks have an efficiency of only from 50 to 75 per cent. The criticisms of expense, difficulty in supplying and laundering and the tediousness of application are not valid arguments when reckoned in terms of protecting the lives of babies. Far from abandoning the face mask, efforts should be directed toward more efficient ones. The use of sheer-gauze masks and of the paper masks should be eliminated in favor of those of more adequate construction, such as the absorbing or the deflector variety.

Epidemic diarrhea of the newborn. The recognition of epidemic diarrhea of the newborn is recent, most of the literature relating to it having appeared within the past decade. In general, the epidemics have had a significant mortality rate.

One of the problems in the control of epidemic diarrhea is the establishment of the diagnosis. Often the first cases develop so insidiously that the possibility of epidemic diarrhea is not considered and proper isolation is not provided until many other infants in the nursery have been exposed to the infection. Anderson and Nelson[31] recognize that there is often a tendency for loose and frequent stools, that overfeeding and improper artificial feeding may cause loose stools, that breast-fed babies frequently have stools postprandially, that drugs, laxatives and food irritants ingested by the lactating mother may cause loose stools in the infant and that parenteral infection or an enteritis due to dysentery organisms may be the cause of diarrhea. In order to protect other infants, however, they advise the isolation of an infant with diarrhea whenever any of the aforementioned conditions cannot be readily incriminated, as well as the provisional diagnosis of epidemic diarrhea of the newborn whenever two or more infants are similarly affected.

Tyson[32] finds it difficult to decide whether epidemic diarrhea is a disease entity in itself or part of a symptom complex. In three epidemics he observed, three different organisms were cultured from both the stools and the blood stream — *Streptococcus haemolyticus*, *Pseudomonas aeruginosa* (pyocyaneus bacillus) and *Escherichia coli* (colon bacillus).

Although a virus etiology for many of the epidemics of diarrhea in the newborn has been suspected it remained for Buddingh and Dodd[33] to demonstrate a virus in one epidemic. These authors had been studying a stomatitis of infants and children that was often accompanied by diarrhea and had demonstrated a hitherto unrecognized virus isolated from the mouths and stools by inoculation of the scarified rabbit cornea. In October, 1943, one of a pair of premature twins in a nursery was found to have stomatitis and diarrhea. Within the next few days several other infants developed the infection. In spite of immediate strict isolation precautions, 16 of the 30 infants in the nursery developed diarrhea within the course of the next two weeks. Although a mild stomatitis was present in 10 of the 16 infants, the outstanding feature of the diseases was diarrhea. Swabs obtained from the mouths and stools of all the affected infants produced characteristic lesions when inoculated upon the cornea of a rabbit. Swabs from the 14 unaffected babies produced no lesion.

Mouth swabs from 3 of the 4 nurses in charge of the nursery were also found to be positive for the virus. Two of the nurses at no time had lesions in

their mouths, but the third developed stomatitis during the week following the outbreak of diarrhea in the nursery. She carried the infection home to her own children, who were six and eight years old, and three months later her mouth swabs were still positive for the virus. Mouth swabs from 2 of 60 adults who were more or less directly engaged in caring for children in the nurseries and pediatric wards were positive for the virus without any accompanying symptoms. One of these carriers was an intern who had taken charge of the nursery after the epidemic of diarrhea had ceased. Four days later 3 new cases of stomatitis and diarrhea developed. Substitution of this intern for another, known to be free of virus, and isolation of the 3 infants controlled further spread of the disease.

When confronted with the possibility of an epidemic of diarrhea in the newborn, time is a factor and treatment cannot wait for the results of laboratory investigation. The plan of treatment at both the Boston Lying-in and Children's hospitals[34] calls for an immediate threefold system of isolation: physical isolation of infected patients; physical isolation of all contacts; and physical isolation of all new admissions from contact with either of the two preceding groups. Active treatment of infected patients is based on the suggestions of Twyman and Horton,[35] which are as follows: succinylsulfathiazole (sulfasuxidine) 1 gr. per pound of body weight per day; opiates by mouth; vitamin K; plasma or whole-blood transfusions; parenteral fluids; and protein milk formulas. In addition to the above procedures the infants are given from 12,000 to 24,000 units of penicillin per day in divided doses every three hours. The rationale of this treatment is that the sulfasuxidine combats enteric infection, if present, that the penicillin combats parenteral infection, if present, and that, if the disease proves to be of virus origin, nothing of a specific nature can be done beyond the general supportive measures outlined. The justification of this "shot-gun" approach is the high mortality associated with diarrheal disease.

In the epidemic of diarrhea of the newborn studied by Anderson and Nelson[31] a low carbon dioxide combining power of the blood was observed in 50 per cent of the cases in which abnormal clinical manifestations were noted, in spite of the fact that most of these infants did not exhibit the classic picture of acidosis. Significant clinical improvement attended the correction of the acidosis by the parenteral administration of a 5 per cent solution of sodium bicarbonate or of a M/6 solution of sodium lactate. They emphasized the importance of constant observation of the ill infants and on the determination of the carbon dioxide level of the blood whenever there are evidences of increasing severity of the disease, with or without the usual manifestations of acidosis.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor**

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CASE 31021

PRESENTATION OF CASE

A fourteen-year-old boy was admitted to the hospital because of abdominal pain and convulsions.

Three weeks prior to admission, while playing football, he was kicked in the right eye. Although he felt dizzy, he did not lose consciousness and was able to resume play. His eye subsequently became swollen and ecchymotic. During the following week he complained a good deal of abdominal discomfort and took soda for relief. About a week later, one week before entry, he was awakened from sleep by severe abdominal pain accompanied by nausea and vomiting. He was given an enema and on getting out of bed appeared confused and unable to find the door. While straining to expel the enema he suddenly became stiff, breathless, cyanotic and then limp and unconscious. He regained consciousness after five minutes. He was not incontinent and did not bite his tongue. There was no headache following the seizure, and he had no recollection of what had occurred. He was admitted to a community hospital where four similar attacks occurred during the next twenty-four hours. He vomited large amounts of dark-brown material. Although he failed to move his bowels for three days, an enema at the end of that time produced good results. The white-cell count was reported to be 19,000, and a roentgenogram of the abdomen was said to show dilated loops of small intestine. He was transferred to this hospital for study.

Physical examination revealed a pale, lethargic but oriented boy in no acute distress. There was slight ecchymosis around the right eye. The pupils, ocular movements, visual fields and fundi were normal. The heart and lungs were negative. The abdomen was tense, distended and tympanitic, with some tenderness and audible peristalsis in the lower abdomen. Neurologic examination was essentially normal.

The temperature was 99.2°F., the pulse 118, and the respirations 20. The blood pressure was 140 systolic, 80 diastolic.

Examination of the blood revealed a hemoglobin of 12.8 gm. per cent. The urine had a specific gravity of 1.022, with a + test for albumin; the sediment contained an occasional red and white cell and a rare hyaline cast per high-power field. The blood serum nonprotein nitrogen was 23 mg. per 100 cc., and the protein 6.4 gm. per 100 cc., with an albumin-globulin ratio of 2.6; the serum chloride was 86 to 96 milliequiv. per liter. A blood Hinton test was negative.

Roentgenograms of the abdomen revealed several dilated loops of small bowel extending across the midabdomen. Considerable gas was seen in the colon but none in the rectum. A barium enema passed without delay from rectum to cecum and revealed no abnormality of the colon. The appendix was negative. The terminal ileum filled for a distance of 5 cm., at which point the barium column terminated rather abruptly; a post-evacuation film showed moderate contraction of the colon, but no further retrograde passage of barium in the terminal ileum. An x-ray examination of the skull was negative.

A Miller–Abbott tube was inserted into the duodenum with some difficulty and several hundred cubic centimeters of fluid was aspirated. After intubation, x-ray films failed to reveal the dilated loops of small bowel previously observed. The nausea and vomiting continued; the urine output was low, and fluids were administered parenterally. Except for the expulsion of the barium enema, the patient did not move his bowels after entry into the hospital. On the night of the fifth hospital day he awakened suddenly with a cry and complained of burning pain in the upper abdomen accompanied by a bearing-down sensation as if he wanted to move his bowels. The temperature rose to 102°F., and the abdomen was boardlike and acutely tender. An emergency laparotomy was performed that night.

DIFFERENTIAL DIAGNOSIS

DR. ARTHUR W. ALLEN: May we see the x-ray films before we start the discussion?

DR. MILFORD SCHULZ: This film, taken shortly after entry, shows the dilated loops of small bowel. There is a little gas in the colon here and there, but the colon is not dilated. On the film made after filling the colon with barium, you can still see the gas in the bowel; the small bowel is dilated but the terminal ileum is not. It is interesting that the appendix, which is filled, apparently is movable — at least the relation between the appendix and the cecum changed following evacuation. In the film taken three days later there is still a residue of barium in the bowel and most of the small bowel has been deflated.

DR. CHESTER M. JONES: Where is the Miller–Abbott tube? In the upper ileum?

DR. SCHULZ: I should say that it was either in the proximal ileum or in the distal jejunum.

DR. ALLEN: I wonder how he knows that.

*On leave of absence.

DR. JONES: That is what I wonder.

DR. SCHULZ: It is not in the distal ileum because it is not near the cecum and there is quite a bit of tube present for it to be in the proximal jejunum.

DR. JONES: I agree.

DR. ALLEN: Having just listened to an excellent discussion of a patient who had two lesions,[1] one wonders whether, by any chance, luck will hold and whether this boy also had two conditions. It is difficult for me to connect his apparently minor injury to the orbit during a football game with the gastrointestinal story. When I first read the abstract I thought that this might well have been a serious injury to the head and that this boy might have had a Cushing syndrome of peptic ulcer on a central-nervous-system basis. As I read farther I thought that he might conceivably have had a peptic ulcer associated with a Meckel's diverticulum containing gastric mucosa. During the week following injury he had a sufficient amount of abdominal discomfort to take soda, and it says "for relief" not "with relief"; one wonders whether this boy did have something that caused gastric hyperacidity.

He got on extremely well, however, until about a week later, that is, two weeks after injury and one week before entry, when he was awakened from sleep by severe abdominal pain accompanied by nausea and vomiting. If he had an ulcer of the stomach that had actually perforated he certainly would have been awakened from sleep. He might have been nauseated and he might have vomited, but it does not appear that he was quite ill enough or that the onset was quite sudden enough for it to be a perforation of an ulcer.

The fact that he was confused following an enema and then had a so-called "convulsion,"—he is said to have become stiff, breathless, cyanotic and then unconscious, — is not particularly helpful because a considerable number of people faint after an enema. It is not unusual for persons to be confused in the middle of the night if they are sleepy, and they might even take the wrong turn and go through the wrong door under these circumstances. We had a man brought in here a few years ago who had just returned from his summer place, where the bathroom entrance was to the left; on arising at night, he, out of habit, turned in this direction instead of to the right, where his town-house bathroom was located, and stepped into an elevator well, falling four flights.

The patient we are discussing here was admitted to a community hospital and had four similar attacks. I suppose that means that he had four periods of unconsciousness. I do not know whether the phrase "similar attacks" means that he also had an enema and severe pain, but I assume that he did not have an enema each time he lost consciousness. He did vomit large amounts of dark-brown material. That may be significant since, if he had a perforated viscus, he would not vomit large amounts of this material unless the perforation was low in the gastrointestinal tract. It is possible that this dark-brown material contained blood, because a patient who is vomiting a good deal will have a certain amount of bleeding from the mucous membranes. On the other hand one wonders if, by any chance, this was small-bowel content that was being vomited. The fact that the enema at the end of three days produced a good result from the colon is of no help except to say that the disease was not in the colon. It only means that he had an accumulation of fecal matter in the colon that had been there prior to the acute illness and that the enema removed some of this fecal material. During the period that he was in the community hospital the white-cell count was said to have been 19,000. We have no mention of white-cell counts after admission here, but I am sure that they were done and should like to know what they were.

DR. BENJAMIN CASTLEMAN: None are recorded.

DR. ALLEN: Of course they were done, but sometimes they do not get recorded. At any rate I shall assume that the count before entry was a comparatively correct figure. It is reasonable to suppose that a secondary inflammatory process was going on, some process that was damaging or at least impairing the blood supply to some segment of the bowel. I suspect that the increased white-cell count was not due to the "black eye."

The physical examination does not help us much, except that at the time he was examined he was not in acute distress, which means that he did not have a continuing process but something that came and went to some extent. That practically rules out the possibility of his having a perforation of a high viscus, unless one can conceive of a perforation that sealed itself off and reperforated; I doubt that this could recur so many times as is described here.

We shall have to accept the fact that neurologic examination was essentially normal. I do not know whether "essentially" is put in for a reason or whether it was entirely normal. There is one small fact — a systolic blood pressure of 140 is abnormally high for a boy of fourteen. He had a slight amount of albumin in the urine and an occasional hyaline cast, both of which might go with an illness of this severity; also there was abnormality in the albumin-globulin ratio, which could have been due to dehydration. The chloride was slightly low.

We know from the roentgen films of the abdomen that he had small-bowel obstruction of some sort. From the film after the barium enema I have to deduce that the obstruction was fairly low in the ileum; the barium certainly stops short at that point as if there were a string around the bowel, or a tumor or gallstone blocking it in that region. It might have been due to a tight band across the bowel. Certainly this is an extremely sharp demarcation in the barium column and therefore suggests a complete, total obstruction at that point.

The patient was observed for a period of five days and did well with Miller–Abbott decompression of the small intestine. We now have reached a point nine days after the acute onset of the abdominal difficulty and four weeks after the football injury, and it is difficult for me to visualize any injury to the abdomen that took place in the football game that would produce this picture. It is also difficult for me to associate the minor injury to the orbit with anything going on later, particularly with a negative neurologic examination and a negative skull plate. So I believe that this sudden episode that happened on the night of the fifth hospital day was something different, probably a complication of the intestinal obstruction. I assume that the sudden pain with a bearing-down sensation was due to a perforation in this region or at least to an extravasation of fluid into the pelvis, since this type of irritation is sometimes seen in acute episodes. Often when an acutely inflamed appendix is lying in the pelvis a patient has exactly this same bearing-down feeling, a desire to move the bowel, usually with no relief.

So in summing up this case I believe that this boy's football injury had nothing to do with his abdominal difficulty. He did have a contusion to his orbit, but he coincidentally began to get into gradual difficulty with his abdomen; this was something rather severe that ended in total small-bowel obstruction in the region of the terminal ileum. This picture probably could not be due to a Meckel's diverticulum. If this boy had an inflammatory process from a Meckel's diverticulum, there would almost surely be a tendency to fill some of the terminal ileum after evacuation of the barium enema. I do not know what could cause this sudden obstruction, but I think that there are two possible explanations. One is that he had a band of adhesions across this area that produced obstruction at this point. I should expect, however, if that had been the case, that he would not have got along so well as he did for the first four days of his illness, that is, before the Miller–Abbott intubation. The only other thing that I can think of to explain such a picture in a boy of this age — obviously it could not have been gallstone ileus, at least I do not believe that it could have been — is that he had an intussusception of the terminal ileum, which is most unusual. Ordinarily intussusception occurs from the ileum into the cecum, but small-bowel intussusception has been reported: Dr. Harvey Stone,[2] of Baltimore, has recently reported a case in which a polyp of the small intestine produced intussusception of the small bowel with obstruction. I believe that is a likely possibility in this case. I can go no farther, however; I believe that the football injury and the small-bowel obstruction were independent.

Dr. Leland S. McKittrick: Dr. Schulz, would the abrupt cessation of the barium in any way suggest that the obstruction was due to intussusception?

Dr. Schulz: Ordinarily, the barium runs around the intussusceptum for a short distance or one can see the leading tumor in the barium. Usually it does not cut off so abruptly as this.

Dr. Allen: This boy probably had an unusual amount of edema around the area, owing to the four days of obstruction prior to the barium enema.

Dr. Schulz: Yes; I presume that it would take some effort to cause barium to run through such an area of intussusception.

Dr. Allen: Do you often see an area as completely trapped as the one shown here?

Dr. Schulz: It is possible. Will a diverticulum loop itself around the bowel?

Dr. Allen: Yes. A diverticulum can do almost anything. Most of the patients with Meckel's diverticulum are operated on under the diagnosis of intestinal obstruction.

Dr. Castleman: But the obstruction is higher up.

Dr. Allen: Yes, but usually close to the ileocecal valve. I do not believe that it was a diverticulum.

Dr. Castleman: Dr. McKittrick operated on this boy. Will you tell us about your findings?

Dr. McKittrick: As Dr. Allen has said, this case was puzzling. We followed through essentially the same line of reasoning, but since we were not up before a clinicopathological conference, we did not have quite the same urge to explain the cause of an obstruction that was obvious when one saw the x-ray films. We had a little trouble with the Miller–Abbott tube, but it did pass the pylorus and did a good job of deflating him. On the afternoon before operation, the abdomen was quite soft and nontender, and I thought that he was doing extremely well. I was called at about four o'clock the next morning because the patient had been awakened by sudden pain. I came down and operated on him with a working diagnosis of acute small-bowel obstruction with perforation. We had not committed ourselves to the cause of the obstruction.

There was a slight delay in getting under way, through no fault of anyone in particular, but it was approximately two hours after the perforation when the abdomen was opened. The peritoneal cavity did not contain so much fecal material and intestinal contents as I had anticipated. There was widespread purulent material and obvious generalized peritonitis. A distended edematous small bowel presented itself, and by putting the hand into the abdomen I could feel the point of obstruction. As gently as I could I lifted it out and saw two open ends, the small bowel being completely divided. How much of that I had done and how much had been done in the small hours of the morning I do not know. It is quite possible that the balloon of the Miller–Abbott tube saved this boy's life by preventing the escape of the small-bowel contents into the abdominal cavity. It not only had deflated the obstructed segment but the tube, being still inflated

and located 5 cm. above the perforation, had acted as a cork to prevent complete emptying of the bowel into the peritoneal cavity.

We, too, were intrigued by the abrupt cessation in the passage of barium. We did not know what it meant. At operation the obstruction was well above the ileocecal valve and had nothing to do with the x-ray finding.

DR. ALLEN: That was the red herring.

DR. MCKITTRICK: There were lymph nodes up to 1.5 cm. in diameter and a great deal of edema. I thought that the boy had a tumor of the small bowel that had ulcerated through. We resected the segment of ileum and did an end-to-end anastomosis, closing the abdomen without drainage. He was given sulfadiazine intravenously. A pelvic mass developed but cleared up without operation. The wound remained clean, and he had an uneventful convalescence. I should like to re-emphasize the fact that the Miller–Abbott tube with the distended balloon going to the point of obstruction and occluding the outflow of material from above probably saved this boy's life.

CLINICAL DIAGNOSIS

Acute small-bowel obstruction, with perforation.

DR. ALLEN'S DIAGNOSIS

Subacute small-bowel obstruction, with gangrene and perforation, probably from intussusception.

ANATOMICAL DIAGNOSIS

Ileoileal intussusception, with gangrene and perforation.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The specimen we received showed a large porky mesentery, as Dr. McKittrick mentioned, which was composed of inflammatory edematous fat. The tumor-like mass in the ileum proved to be an intussusception of 7 cm. of the ileum, which had become gangrenous. That is why it broke in half. I believe that the boy had it at the time of the first attack of abdominal pain, three weeks before he was operated on, and that that accounted for the extreme necrosis of the bowel, which was black.

DR. MCKITTRICK: I just asked Dr. Allen if he had ever seen an intussusception of the ileum without something to lead it.

DR. CASTLEMAN: We sectioned the entire specimen and could find no evidence of tumor. It is possible that there had been a polyp, but the bowel had become so gangrenous that we could not recognize it.

DR. ALLEN: It might have sloughed off.

DR. CASTLEMAN: That is possible, but there were no polyps elsewhere in the specimen.

DR. ALLEN: I would like to take issue with you on the statement that this intussusception had existed for four weeks. It is possible to get dead gut in a matter of four days. Is it not possible that this boy had intermittent intussusception during the first three weeks of his sickness, which was at least two weeks before he finally became completely obstructed? His complete obstruction, I believe, dates from the night he was awakened with the severe abdominal pain.

DR. CASTLEMAN: I think that is true. I did not mean that he had complete obstruction for four weeks but that he had intermittent intussusception during this period, with frequent injuries to the ileum in the region of the intussusception.

DR. JONES: Can you recall how many cases you have had with true ileal intussusception without a tumor?

DR. CASTLEMAN: It must be extremely rare. I do not recall another case, but as Dr. Allen mentioned, the tumor may well have sloughed off.

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CASE 31022

PRESENTATION OF CASE

A forty-three-year-old woman was admitted to the hospital with dysphagia and headache.

The patient was in apparent good health until two and a half months prior to admission, when she noted difficulty in swallowing liquids. Attempts to drink milk, for example, were followed by choking and she had difficulty in getting her breath. The dysphagia was not always present, and she apparently had no difficulty in swallowing solid foods. She also noticed that her voice was weak and hoarse. Lying down at night brought on a feeling of oppression in the chest, which was not relieved by sitting up. A sense of obstruction was present in the throat, resulting in constant unproductive attempts to clear the throat. There was no cough or expectoration. Three weeks before entry she developed a severe pounding headache aggravated by motion. It was worse in the morning, often beginning as a generalized throbbing and finally localizing in the right temple. Two weeks prior to admission she noted marked weakness of the right arm and was unable to control its movement when reaching for things. The legs felt stiff, and she seemed unable to lift them. Sharp pains were present in the left leg. About four months before admission the patient had several episodes of pain and fullness in the epigastrium that came on about an hour after meals. The distress was relieved to some extent by a hot-water bottle but not by food. A local physician made a diagnosis of gastric ulcer by fluoroscopy. Following treatment the symptoms

disappeared, and at the time of admission she had been free of epigastric distress for three months.

Physical examination revealed a poorly developed, emaciated and dehydrated woman with a weak, hoarse voice. The breasts were poorly developed but otherwise negative. There was no adenopathy. The pupils reacted to light and accommodation. The gait was shuffling. The Romberg sign was positive. The right shoulder drooped and could not be raised; the muscles of the right shoulder and upper arm showed hypotonicity and some atrophy. There was a tendency toward "winging" of the right scapula. All the deep tendon reflexes were hyperactive, more so on the right. The right lower abdominal reflex was diminished. The plantar responses were flexor in type bilaterally. The finger-to-nose and heel-to-knee tests showed awkwardness and overshooting bilaterally, but more so on the right.

The temperature was 98.6°F., the pulse 94, and the respirations 20. The blood pressure was 116 systolic, 70 diastolic.

Examination of the blood showed a red-cell count of 4,520,000, with 14 gm. of hemoglobin, and a white-cell count of 8500, with 60 per cent neutrophils. The urine and stools were negative. The serum protein was 6 gm. per 100 cc.; the blood sugar and the serum nonprotein nitrogen were normal. A tuberculin test in a dilution of 1:1000 was negative. A Hinton test was negative.

A roentgenogram of the chest revealed a few linear shadows in the left third and fourth interspaces anteriorly. An ill-defined shadow was present in the region of the left hilus. An x-ray examination of the skull was negative. Two electroencephalograms taken soon after admission revealed a diffuse spotty dysrhythmia without consistent focal distribution but generally worse toward the occiput.

A lumbar puncture revealed clear colorless fluid. The pressure was normal initially and responded normally after jugular compression. No cells were present; the protein content was normal, and the Wassermann test was negative. An examination of the larynx revealed complete paralysis of the left vocal cord, which lay in the so-called "cadaveric position." The right cord functioned normally.

On the twentieth hospital day the temperature gradually began to rise, reaching 102°F. over a period of about thirty-six hours. She developed some cough, raising a small amount of sputum, and there was pain over the left anterior chest on coughing. The left apex and upper chest were dull to percussion, with bronchial breath sounds anteriorly and an expiratory grunt. There were coarse rales over the left apex posteriorly. The liver was palpable two fingerbreadths below the costal margin. A sputum culture revealed alpha-hemolytic and a few beta-hemolytic streptococci, and a blood culture was negative. The white-cell count was 24,000. A catheterized urine specimen was negative. A roentgenogram of the chest revealed irregular patchy consolidation of the left upper lobe and a small amount of fluid in the posterior costophrenic sinus.

The temperature continued to range between 100 and 102.6°F. Respirations were shallow and rapid, and the patient appeared dehydrated and slightly cyanotic. She was treated with sulfadiazine and oxygen. On the twenty-sixth hospital day, the patient became jaundiced and a moderate amount of bile appeared in the urine. Sulfadiazine was stopped and penicillin substituted. She was also given potassium iodide because of difficulty in bringing up the tenacious sputum. Diffuse coarse rales were audible throughout the lung field.

On the thirtieth hospital day the patient began to improve. The temperature gradually fell to normal, and the sputum diminished in quantity. The icterus cleared completely, and the liver was no longer palpable. The lungs showed slight dullness over the entire left chest, with scattered fine and coarse rales, and normal breath sounds diminished over the left apex anteriorly. There was slight sacral edema. The total plasma protein was 5.3 gm. per 100 cc., with an albumin-globulin ratio of 0.93. The serum chloride was 90 milliequiv. per liter. A cephalin flocculation test was negative in twenty-four and $\pm$ in forty-eight hours. X-ray examination of the chest revealed little change in the appearance of the left upper lobe.

The temperature continued to range between normal and 100°F., occasionally reaching 101°F. The neurologic signs originally noted became more marked, with extreme weakness of the right arm. A positive Hoffmann sign appeared on the right, but the Babinski signs were negative. Dullness and bronchial breath sounds reappeared over the left upper lobe and were accompanied by scattered fine rales and a cough, which was moderately productive of purulent sputum. Another chest film revealed no change in the left upper lobe, but the right lung field showed increased linear markings. Pleural fluid was present bilaterally. Several convulsions of the Jacksonian type occurred, each lasting several minutes. The convulsive movements started in the right hand and arm, spreading to the leg and face. The seizures were followed by drowsiness and sleep. On the fortieth hospital day a Babinski sign was elicited on the right and there was prolonged ankle clonus on the right. There was dullness to pinprick in the right leg. On the same day the patient had a convulsion followed by temporary aphasia.

She continued to cough and raise large quantities of green mucoid sputum. She became unco-operative, refusing all food and medication. The chest signs continued unchanged. She became extremely weak and drowsy and expired on the fifty-third hospital day following a convulsive episode.

Differential Diagnosis

Dr. Arthur Linenthal: The problem in this patient appears to be one of disease involving structures within the chest as well as the central nervous

system. Consideration of the neurologic lesion may appropriately follow discussion of the chest difficulty, since I think that the two are interrelated.

The presenting symptoms of this patient were difficulty in swallowing, difficulty in breathing, a sense of oppression in the chest, a sense of obstruction in the throat, and weakness and hoarseness of the voice. The complete paralysis of the left vocal cord, fixed in the cadaveric position midway between phonation and quiet inspiration, and the ill-defined x-ray shadow in the left hilar region suggest that these findings as well as the symptoms may have been due to some process in the left hilar region involving the left recurrent laryngeal nerve and pressing on the esophagus and trachea. The emaciated condition of the patient on admission is consistent with the impression that a malignant neoplasm was the likeliest basis of such a process.

Regarding the primary site of such a tumor, bronchiogenic carcinoma seems most probable, although other locations must be considered. It is interesting that there had been no cough and no sputum before the patient entered the hospital, but this does not rule out a pulmonary neoplasm.

The statement that a gastric ulcer had been seen by fluoroscopy raises the question whether there was a gastric neoplasm with metastases to the hilar nodes and surrounding structures. Since the abdominal symptoms that led to the fluoroscopy subsided, x-ray studies of the stomach were not repeated, and we have no evidence on which to settle this question.

There is no evidence for other diseases that might have given rise to the presenting symptoms and physical findings. Neither physical examination nor x-ray examination showed evidence of an aortic aneurysm, and examination of the larynx did not reveal any intrinsic disease. Esophageal carcinoma might well have explained the presenting picture, but since no studies of the esophagus were made, there is no way to confirm this diagnosis.

At the end of the third week in the hospital, the patient developed a pulmonary infection in the left upper lobe. This was marked by fever, cough, sputum and pain over the left chest. The respirations were rapid and shallow, and she became cyanotic. Physical examination gave evidence of consolidation over the left upper lobe, and this was confirmed by x-ray. Elevation of the white-cell count suggests a bacterial etiology, but the sputum showed only alpha-hemolytic and a few beta-hemolytic streptococci. She was given sulfadiazine and then penicillin, but there is no evidence that these were of value. The patient improved, the physical findings over the left upper lobe diminished but never entirely disappeared, and the x-ray picture showed little change.

It is interesting that this severe pulmonary infection developed in the left upper lobe, since the lesion that I have supposed to exist at the left hilus could easily have compressed the left upper lobe bronchus and caused some increased susceptibility to infection in that area. The linear shadows seen in the third and fourth left interspaces on the first chest film may have represented small areas of atelectasis.

At the time of the development of the pulmonary infection, before the patient had received any chemotherapy, the liver was found to be enlarged. Subsequently she was given sulfadiazine, and while receiving the drug, she became jaundiced and had bile in the urine. The sulfadiazine was stopped and soon afterward, along with improvement in the pulmonary condition, the jaundice disappeared and the liver became smaller.

It is difficult to be sure of the relation between the pulmonary infection, the sulfonamide therapy and what appears to have been an episode of acute hepatitis. Toxic hepatitis has been described after sulfadiazine, but the presence of the hepatic enlargement in this case before sulfadiazine was given makes me believe that the sulfa drug was probably not responsible. Bacterial pneumonia may be accompanied by jaundice. There is also the possibility that both the pulmonary infection and the hepatitis were due to a virus infection. The negative cephalin flocculation test done at about the time the jaundice was subsiding suggests that the degree of liver damage was slight. No other liver function tests were done. The plasma proteins showed no significant change.

Obstructing lesions of the biliary tract must be mentioned, but there is nothing to support such a diagnosis and the transient hepatic enlargement is suggestive of intrahepatic disease. There was apparently no abdominal pain at that time, and there is no evidence for gallstones. Metastatic disease of the liver or around the bile passages seems too remote to be seriously considered.

The pulmonary infection never entirely cleared up, and indeed at the time of death there was an increase in the physical findings, as well as a persistence of the x-ray abnormalities over the left upper lobe and the development of purulent sputum. Apparently the infection was a persistent one, either because of some blockage of drainage from the involved lobe or because of the characteristics of the infectious process. This may well have been a virus disease with superimposed bacterial infection.

The acuteness of the onset of the pulmonary infection, together with the absence of clinical or x-ray evidence of pulmonary tuberculosis on admission, seems to eliminate tuberculosis as a possibility. Unfortunately there is no record of a search for tubercle bacilli in the sputum.

The neurologic disorder was, I think, related to the disease in the chest; that is, it was caused by a metastasis of the malignant process. The problem

here is to decide on the basis of the evidence presented how many neurologic lesions were present and where they were located.

The terminal neurologic findings were marked. The weakness in the arm, the appearance of a Hoffmann sign, the development of Jacksonian convulsions starting in the right arm and hand, the appearance of a Babinski sign on the right with ankle clonus, the increase in the deep tendon reflexes on the right and the episode of temporary aphasia point to a lesion in the left cerebral hemisphere involving primarily the motor area for the arm with extension to the motor area for the leg and to the nearby speech area. Sensory changes, such as the late dullness to pinprick in the right leg, suggest subcortical extension of the process.

The earliest manifestation of any neurologic disorder was the development of weakness in the right arm. Subsequently the muscles of the right arm and the right shoulder girdle showed atrophy. This finding suggests a metastatic lesion involving the anterior-horn cells of the right side of the mid-cervical spinal cord. There was hypotonicity, but the deep tendon reflexes were also increased. The atrophy can be explained on the basis of weakness of the right arm with resulting disuse. The stiffness in both legs at the onset is difficult to explain. The positive Romberg sign and the evidence of incoordination on admission may be attributed to weakness. It seems, therefore, that all the findings can be explained on the basis of one metastatic cerebral lesion.

The patient went down hill rapidly and died following a convulsive seizure, probably owing to involvement of a vital nervous center.

Clinical Diagnoses

Tumor involving left motor cortex of brain (? primary, ? metastatic from bronchiogenic carcinoma).
Unresolved pneumonia: left upper lobe.

Dr. Linenthal's Diagnoses

Bronchiogenic carcinoma of left lung, with metastases to regional nodes and left cortical and subcortical regions of brain.
Unresolved pneumonia: left upper lobe.
Acute hepatitis, subsiding.

Anatomical Diagnoses

Carcinoma, oat-cell type, of left upper lobe, with metastases to bronchial, mediastinal, mesenteric and retroperitoneal lymph nodes, liver, kidney and brain.
Chronic pneumonitis: left upper lobe.
Bronchiectasis: left lower lobe.
Cerebral pressure cones.

Pathological Discussion

Dr. Benjamin Castleman: As Dr. Linenthal predicted, the pulmonary and cerebral lesions were related. This woman did have a bronchiogenic carcinoma, the primary focus being in the bronchus to the left upper lobe, which was completely occluded. The metastatic bronchial and mediastinal lymph nodes had infiltrated the wall of the left main bronchus, especially the lower lobe bronchus. The latter was so narrowed that secondary bronchiectasis had developed throughout the lower lobe, the bronchioles being dilated and filled with purulent material. The primary tumor in the left upper lobe had extended into the parenchyma around the bronchus for about 4 cm., and the remaining pulmonary tissue in this lobe was gray and rubbery, characteristic of the so-called "drowned out" or "stasis" pneumonitis.

There were three cerebral metastases. The largest, and the one that caused most of the cerebral symptoms, was a cystic lesion measuring 6 by 3 by 2.5 cm. in the left parietal region. The other two, each about 2 cm. in diameter, were solid nodules, one in the right posterior frontal region and one in the posteroinferior portion of the right cerebellar hemisphere. There was definite evidence of increased intracranial pressure, as shown by flattening of the convolutions and the deep cerebellar and temporal pressure cones.

The liver weighed over 2000 gm. and contained many metastatic nodules. I do not believe, however, that there was sufficient replacement of parenchyma to have produced even the transient jaundice. A likelier explanation is the presence of many metastatic lymph nodes surrounding and compressing the common bile duct.

Microscopically the carcinoma was extremely undifferentiated, showing no tendency to either keratinization or gland formation. In many places it suggested the oat-cell type.

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NOT SO GOOD

Two federal agencies that seem to have had some difficulty in retaining the confidence of the public, and between which close harmony is essential although its existence is not always apparent, are the War Food Administration and the Office of Price Administration. A duty of the WFA, through its carefully organized system of food experts, is to know month by month, as well as year by year, the food resources of the country and their proper allocation to the armed services, to lend-lease and to the civilian population. A function of the OPA is to effect and maintain a system of food rationing that will provide an equitable distribution of the country's resources so far as native intelligence and human honesty can assure it.

An example of the failure of these two agencies to co-ordinate their activities was furnished last fall when the WFA made public announcement that twelve pounds of butter per capita per year was available to the entire civil population. At that time butter was worth twenty red points per pound on the rationing list, and since each individual had available thirty points for each four-week period, no slide-rule expert was needed to apprise the concerned housewife of the fact that in order to obtain her promised butter she must give up two thirds of the points that also had to cover her expenditures for meat, cheese and other fats. As of Christmas night, moreover, the Magi whose guiding star shines over the Potomac presented a somewhat suspicious public with an increase in the point value of butter to twenty-four, and canceled many outstanding points that the thriftier housewives had been saving against a rainy day.

Thus are prudence and patriotism rewarded, and thus is the bewildered citizen encouraged to disregard the rules, since they have been changed in the middle of the game. As the *Boston Herald* notes in the leading editorial of December 27, 1944: "A government that repudiates its currency forfeits the confidence of its people. We can ill afford to lose faith in the Office of Price Administration, but its action in canceling certain unspent red, blue and sugar stamps is unpleasantly akin to currency repudiation."

It is not implied that butter is an essential kind of food; we can do without butter, as many of us have already learned. What we cannot dispense with is confidence in the agencies that are attempting to lead us through our wilderness. Probably the worst that can be said is that, like some of our military leaders, they simply did not know what was going on. In that lack of knowledge, however, they have lost face with the public to which they are eventually answerable. This has made it more difficult, moreover, for some of the volunteer citizen aides, such as the members of medical advisory committees, to solve their own problems conscientiously and to retain to any great degree the confidence of their own "public."

This country can double and triple and quadruple the sacrifices that it is making, and may yet have

to do so now that its introductory years to total war are over. It can do so with calm confidence, however, only if it can have faith in the judgment and ability of its leaders, as well as in their integrity; and this last is not being questioned. If democracy at war may be considered as passing through a forest of disillusionment guided only by a flickering lamp of patriotism, then let us at least turn our ingenuity to trimming the lamp and not to extinguishing it.

EARLY DIAGNOSIS OF TYPHUS FEVER

THE medical profession and the lay public of New England are not particularly concerned with typhus fever. This disease is a clinical curiosity in most parts of this country, particularly in New England. In many other parts of the world, however, it is of frequent occurrence and is always a serious problem. Members of our armed forces are now to be found in almost all the countries in which this or similar rickettsial diseases are both endemic and epidemic. The present war has stimulated considerable interest and activity in this field, and great strides forward have been taken in the recognition and prevention of many of the rickettsial diseases. Among the Russian investigators who have made notable contributions is Professor A. A. Smorodintsev, chief of the Virus Disease Division of the All Union Institute of Experimental Medicine in Moscow, who visited this country last year.

One of the most significant aspects of any program of prevention or eradication of an infectious disease is its early recognition. The diagnosis of typhus fever in the past has depended on the Weil–Felix reaction. This is a test for agglutinins against certain strains of the proteus bacillus in the serum of the patient. It depends on the empirical observation that such antibodies appear during the latter part of the illness, and during convalescence, of certain rickettsial diseases, including typhus fever. It is, therefore, not a highly specific reaction. Furthermore, positive results are not obtained until after the fifth day and usually only after the first week.

Smorodintsev and Drobyshevskaya[1] have recently described a complement-fixation test that is designed to detect the presence of antigen in the serum of patients during the earliest stages of the disease. This test, therefore, has the advantage of giving the earliest possible diagnosis and probably is also more specific. It involves the use of suitably chosen convalescent serums from recovered patients, but serums from hyperimmune rabbits will presumably prove equally satisfactory or even better. The test is carried out by mixing immune serum with inactivated serum from the patient in the presence of suitable amounts of complement, and then testing for the fixation of complement with a suitable hemolytic system.

With this test, a positive diagnosis was made in all patients from whom serum was obtained during the first two days of the disease and in about 60 per cent of those from whom the serum was obtained between the third and sixth days of the disease. Positive Weil–Felix reactions did not occur in any of the serums obtained during the first four days of the disease, and this test was positive in only 38 per cent of the serums obtained on the fifth and sixth days. Moreover, between the fifth and eighth days of the disease, positive tests were obtained in one third of the serums only by the complement-fixation test and in another third only with the Weil–Felix reaction, the remaining serums being either positive or negative to both tests.

It is thus seen that in the first days of the disease this complement-fixation test is almost completely reliable, while during the latter part of the first week of the disease and possibly during the early part of the second week, the use of both the complement-fixation and Weil–Felix tests should give a positive diagnosis in at least two thirds of the cases. Although the principle involved in this method — namely, the detection of a circulating antigen early in the course of the disease — is not new, it has never before been applied in exactly this manner. It has been used to detect the type-specific soluble substance of the pneumococcus in the blood of patients early in pneumonia.[2] It has also been used to detect precipitinogen in early cases of yellow fever.[3]

Recent attempts to devise a diagnostic method more useful than the Weil–Felix reaction have resulted in a technic employing a rickettsial antigen prepared from agar tissue cultures in

a complement-fixation test,[4] but it is obvious that such a procedure measures *antibody* rather than *antigen* in the patient's serum and that it is less likely to give a positive reaction early in the course of disease than is a test for antigen.

Since much of the work on typhus fever that has been done by workers in this country and in Great Britain is confidential and has not been published, it is more than likely that extensive observations have already been made with respect to the application of this test and possibly of others that are equally useful. The results of these and other observations will determine whether the test suggested by the Russian workers is a valuable clinical aid, and further study may reveal other virus or rickettsial diseases to which this principle may be adaptable for early diagnosis.

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MISCELLANY

HOSPITALS APPROVED FOR GRADUATE TRAINING IN SURGERY

The American College of Surgeons has recently announced that two hundred and thirty-one hospitals in the United States and Canada have been approved for graduate training in general surgery and the surgical specialties. In announcing the list, Dr. Malcolm T. MacEachern, associate director, states that surveys of five hundred or more hospitals offering opportunities for graduate training in surgery are planned during the coming year, the increased emphasis on this work being stimulated by the need for providing ample opportunities for resumption of training by medical officers when they return from service with the armed forces. The College helps hospitals to organize graduate training programs to meet the requirements for approval, and also plans to aid physicians returning from service in resuming their training in surgery. The list of hospitals in Massachusetts is as follows:

Hospital	Approved Type of Training
Boston	
Beth Israel Hospital (215 beds)	General surgery Urology
Boston City Hospital (2378 beds)	General surgery Neurological surgery Orthopedic surgery Urology
Boston Lying-in Hospital (138 beds)	Obstetrics
Carney Hospital (234 beds)	General surgery Obstetrics and gynecology
Children's Hospital (256 beds)	General surgery Neurological surgery Orthopedic surgery Otolaryngology
Lahey Clinic (New England Baptist Hospital—228 beds) (New England Deaconess Hospital—310 beds)	General surgery Neurological surgery Orthopedic surgery Urology Otolaryngology
Massachusetts Eye and Ear Infirmary (227 beds)	Ophthalmology Otolaryngology
Massachusetts General Hospital (851 beds)	General surgery Neurological surgery Orthopedic surgery Urology
Massachusetts Memorial Hospitals (414 beds)	General surgery Obstetrics
Peter Bent Brigham Hospital (108 beds)	General surgery Urology
Brookline	
Free Hospital for Women (101 beds)	Gynecology
Worcester	
Memorial Hospital (185 beds)	Otolaryngology

CORRESPONDENCE

SIGNED EDITORIALS

To the Editor: Having read the original editorial "Polypharmacy and Anesthesia" with at least marked disagreement to many of the statements in it and certainly with curiosity as to who propounded them I am prompted again to suggest the wisdom of having editorials signed.

I know that this matter has already been once disposed of in opposition and with disapproval of this procedure, but I wish again to call attention to the fact that it would have so placed the responsibility for statements which are so contrary to the opinions of experienced anesthetists that I am certain that the author would have either hesitated to make them or have prepared himself more fully to support them.

It is still my conviction that the signed editorial bears greater weight and causes less confusion and even less harm than the unsigned one, which permits statements that would frequently not be made were it necessary for the author to sign his name to it.

Frank H. Lahey

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BOOK REVIEWS

Homicide Investigation: Practical information for coroners, police officers and other investigators. By LeMoyne Snyder, M.D. With chapters by Captain Harold Mulbar, Charles M. Wilson and C. W. Muehlberger. 8°, cloth, 287 pp., with 116 illustrations. Springfield, Illinois: Charles C Thomas, 1944. $5.00.

The purpose of this book in the words of its author is "to make available to coroners, police officers or others, whose duty it is to inquire into the nature of a homicide, tested practical plans of procedure to follow in adequately investigating the death." He refers to it as a synopsis of factual information intended to be of practical use to men without scientific training whose duties call them to investigate potentially violent deaths.

The book is well illustrated and written in simple language. It is particularly valuable in that it teaches what not to do as well as what to do. It covers the needs of the coroner or medical examiner who is isolated from larger centers, and also the progressive police chief. It includes a consideration of the value of methods of lie detection, based on the use of the Keeler polygraph, which is looked on as a valuable aid to crime detection. The work can be highly recommended as a practical guide for those for whom it is intended.

Practical Malaria Control: A handbook for field workers. By Carl E. M. Gunther, M.D., B.S., D.T.M. (Sydney). With a foreword by Prof. Harvey Sutton, O.B.E., M.D., F.R.A.C.P., B.Sc., D.P.H., F.R.San.I. 12°, cloth, 91 pp. New York: Philosophical Library, 1944. $2.50.

The foreword by Prof. Harvey Sutton states that the author of this book, Dr. Carl E. M. Gunther, spent many years at Bulolo in the Mandated Territory of New Guinea as a field medical officer of a gold-dredging company. The seat of operations was in the midst of tropical forests where malignant tertian malaria was highly endemic. Dr. Gunther is an entomologist of repute, and a student of clinical and preventive medicine who is well acquainted with its literature; at present he is with the Australian Medical Corps.

The author offers the booklet in the hope that it may help those who are meeting malaria in the field with only an academic knowledge of the disease. Although adapted to local conditions in New Guinea, the author believes that his methods of dealing with malaria are applicable in other undeveloped districts where the population is widely scattered. The opinions expressed are based on experience gained during a period of ten years. The author recognizes that some of his views are radical, unscientific or dogmatically expressed. Dogmatism is justifiable, however, in so condensed an outline of the broad subject of malaria.

The reviewer finds that some of the author's statements regarding the absorption of quinine are of doubtful validity and that the author is in error when he says that quinine is directly toxic to all types of malaria parasites at all stages (evidently, Dr. Gunther forgot to take the sporozoite into consideration). The paucity of exact knowledge regarding the absorption and the action of quinine and other drugs in malaria, however, justifies differences of opinion.

The text contains many interesting observations. Practical methods of treatment are described in detail. The booklet should be of interest to students and of great value to medical field workers.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Practical Malaria Control: A handbook for field workers. By Carl E. M. Gunther, M.D., B.S., D.T.M. (Sydney), field medical officer, Bulolo Gold Dredging Limited, Territory of New Guinea. With a foreword by Prof. Harvey Sutton O.B.E., M.D., F.R.A.C.P., B.Sc., D.P.H., F.R. San. I. 12°, cloth, 91 pp. New York: Philosophical Library, 1944. $2.50.

Radiation and Climatic Therapy of Chronic Pulmonary Diseases: With special reference to natural and artificial heliotherapy, x-ray therapy and climatic therapy of chronic pulmonary diseases and all forms of tuberculosis. Edited by Edgar Mayer, M.D., assistant professor of clinical medicine, Cornell University Medical College, New York City, attending physician, New York and Memorial hospitals, special pulmonary consultant, New York State Department of Labor, and director (*ex urbe*) Northwoods and Will Rogers Tuberculosis sanatoriums, Saranac Lake, New York. 8°, cloth, 393 pp., with 46 illustrations. Baltimore: Williams & Wilkins Company, 1944. $5.00.

This composite work of twenty-two authors reflects the present-day knowledge of the special treatment of chronic pulmonary diseases, including all forms of tuberculosis. Incorporated in the work are the clinical experiences of the editor and of many of the collaborators.

Technique in Trauma: Planned timing in the treatment of wounds, including burns, By Fraser B. Gurd, M.D., C.M., and F. Douglas Ackman, M.D., C.M., in collaboration with John W. Gerrie, M.D., C.M., Edward S. Mills, M.D., C.M., Joseph E. Pritchard, M.D., and Frederick Smith, M.D. with a preface by John S. Lockwood, M.D., University of Pennsylvania, and a commentary by Ralph R. Fitzgerald, M.D., C.M. McGill University. 4°, cloth, 68 pp., with 3 plates, 17 figures, 5 tables and 3 charts. Philadelphia: J. B. Lippincott Company, 1944. $2.00.

This small monograph is composed of three articles that appeared in the *Annals of Surgery* in 1942, 1943 and 1944, with some additions to the text. The basis of the monograph is carried on at the Montreal General Hospital. The authors emphasize not only the importance of adherence to the basic physiologic principles, but also bring out the fact that these principles can only be applied to a large hospital by the use of sound planning and thorough teamwork.

Industrial Ophthalmology. By Hedwig S. Kuhn, M.D. 8°, cloth, 294 pp., with 114 illustrations, including 2 color plates. St. Louis: C. V. Mosby Company, 1944. $6.50.

In this book the author attempts to co-ordinate much of the essential information relating to the various ophthalmologic problems that confront industry.

Minor Surgery. Edited by Humphry Rolleston and Alan Moncrieff. 8°, cloth, 174 pp., with 30 illustrations. New York: Philosophical Library, 1944. $5.00.

This new manual in minor surgery is made up of eighteen articles on selected subjects, written by English authorities in their special fields. Although there is not any preface or foreword, it seems evident that this small work is published at this time for war reasons. The editing is well done and the various articles are short, emphasizing diagnosis and emergency treatment. The subjects covered include minor wounds, sprains, the foot and hand, the mouth, nose, throat and eye, bursas and ganglia, certain benign tumors and cysts, skin infections, the rectum, the genitourinary system, nonoperative treatment of hernias and the fitting of trusses and belts, varicose veins, ulcers and phlebitis, gynecology, the surgery of children, and anesthesia in minor surgery.

Virus Diseases in Man, Animal and Plant: A survey and reports covering the major research work done during the last decade. By Gustav Seiffert. 8°, cloth, 332 pp. New York: Philosophical Library, 1944. $5.00.

In this small volume the author attempts to give a survey of the present status of virus investigations with special consideration of the most recent literature, especially that from foreign countries. The work discusses the important virus diseases of man, animal and plant, and its aim is to furnish an introduction to the study of the viruses.

Homicide Investigation: Practical information for coroners, police officers and other investigators. By LeMoyne Snyder, M.D., medicolegal director, Michigan State Police. With chapters by Captain Harold Mulbar, chief of the Identification Bureau, Michigan State Police, Charles M. Wilson, director, Chicago Police Scientific Crime Detection Laboratory, and C. W. Muehlberger, director, Michigan Crime Detection Laboratory. 8°, cloth, 287 pp., with 116 illustrations. Springfield, Illinois: Charles C Thomas, 1944. $5.00.

The War and Mental Health in England. By James M. Mackintosh, M.D., professor of preventive medicine, University of Glasgow. 8°, cloth, 91 pp. New York: The Commonwealth Fund, 1944. 85 cents.

This collection of nine informal essays discusses in nontechnical language mental health in England during the first four years of the present war, with the outlook for the remainder of the war and the postwar period. The author considers the impact of the war on the new soldier, the industrial worker, the hospital patient and the civilian. In discussing the efforts that are being made to safeguard mental health in England the author considers such topics as hospital service and rehabilitation, and professional education. Dr. Mackintosh has long been connected with the mental-hygiene movement in Great Britain, and in these essays he gives a picture of wartime conditions in England.

Stop Worrying and Get Well. By Edward Podolsky, M.D. 8°, cloth, 124 pp. New York City: Bernard Ackerman, Incorporated, 1944. $2.00.

In this small book the author attempts to show how to meet daily problems in a sound way, without putting an undue strain on the mind and the nervous system. The author in a popular way discusses the effects of the mind on the body in health and disease.

Hydronephrosis and Pyelitis (Pyelonephritis) of Pregnancy: Etiology and pathogenesis (a historical review). By H. E. Robertson, M.D., Section on Pathologic Anatomy, Mayo Clinic, Rochester, Minnesota. 8°, cloth, 332 pp., with 11 illustrations. Philadelphia and London: W. B. Saunders Company, 1944. $4.50.

In this historical survey the author has endeavored to present a fairly complete account of all the important work that has been done on dilatation and infection of the ureters in pregnancy. A comprehensive bibliography of 974 references is appended to the text, and all these articles are referred to throughout the work. This small book should prove a valuable reference source to all physicians interested in obstetrics and genitourinary diseases and to all libraries.

Poliomyelitis. By Edward C. Rosenow, M.D. Vol. A 44 of the International Bulletin for Medical Research and Public Hygiene (Editor-in-chief, W. L. Colze). 8°, paper, 87 pp., with 26 illustrations and 16 tables. New York: The International Bulletin, 1944. $2.75.

In this pamphlet Dr. Rosenow summarizes his work on the streptococcal causation of poliomyelitis and the streptococcal source of the virus causing the disease. Dr. Rosenow states that he has succeeded in inoculating *Macacus rhesus* monkeys with his poliomyelitis virus, producing the clinical and pathologic picture of the disease, and completing twenty-seven years' work on the relation of streptococci to epidemic poliomyelitis and its virus. A summary is also given regarding treatment of the disease with antistreptococcus serum, showing that the death rate is greatly lower in patients treated with the serum. A bibliography of 115 references is appended to the text.

Elimination Diets and the Patient's Allergies: A handbook of allergy. By Albert H. Rowe, M.D., lecturer in medicine, University of California Medical School, San Francisco, California, and consultant in allergic diseases, Alameda County Hospital, Oakland, California. Second edition, thoroughly revised. 8°, cloth, 256 pp. Philadelphia: Lea and Febiger, 1944. $3.50.

This new edition has been thoroughly revised, and the entire text reset. The cereal-free elimination diet has been adjusted because of the scarcity of some foods. Indications for the use of fruit-free elimination diet are discussed for the first time. A new special elimination diet for the control of colitis and various supplemental diets for unusual types of food allergy, as well as special diets for obesity and diabetes and for infants and children, are given in detail. All menus and recipes have been revised in the light of rationing and restriction of foods owing to the present war.

Small Community Hospitals. By Henry J. Southmayd, director, Division of Rural Hospitals, the Commonwealth Fund; and Geddes Smith, associate, The Commonwealth Fund. 8°, cloth, 182 pp. New York: The Commonwealth Fund, 1944. $2.00.

This small book outlines the experience of the Commonwealth Fund during the past twenty years in the organization, construction and operation of small community hospitals in various parts of the United States. Persons interested in small hospitals in any of their aspects will find here a frank discussion of all the major questions facing such hospitals. The text lays stress on hospital administration rather than on the hospital plant. However, there is a chapter on building design, covering the broad architectural principles that have been tested in fourteen community hospitals. From an executive point of view the relations of the board of directors, the medical staff, the superintendent and the staff are discussed in sufficient detail to give the beginner a practical understanding of hospital management. In 1925, the Commonwealth Fund embarked on a definite program for the building and operation of small fifty-bed community hospitals, servicing an area of approximately twenty-five to thirty-five square miles. The fund proposed to meet two thirds of the cost of building and equipment, and the communities were to provide suitable sites, responsible management and the necessary maintenance cost. It is thus seen that aid was offered only to communities that would assume a stated share of the capital costs and would guarantee the necessary funds for maintenance and in due time become independent of foundation subsidy or supervision. Under this plan twelve hospitals have been completed, together with a county hospital built before the plan was formerly launched and an older hospital remodeled and reorganized in co-operation with the fund. The hospitals were also required to subscribe to the minimum standard for hospitals of the American College of Surgeons. This small work is aimed directly at the nonprofessional men and women who take the responsibility for the community hospital. It is written in nontechnical language and should be in every small public library in the country.

The Principles and Practice of Ophthalmic Surgery. By Edmund B. Spaeth, M.D., professor of ophthalmology, Graduate School of Medicine, University of Pennsylvania, attending surgeon, Wills Hospital, Philadelphia, consultant in ophthalmology, Philadelphia Hospital for the Insane, Byberry, and assistant ophthalmologist, Rush Hospital, Philadelphia. Third edition, thoroughly revised. 8°, cloth, 934 pp., with 556 engravings, containing 798 figures and 6 colored plates. Philadelphia: Lea and Febiger, 1944. $11.00.

This third edition of a standard work has been revised by the addition of much new material and many new illustrations, thus bringing the contents fully up to date. In view of the unusual demand made on ophthalmologists by the war, emphasis has been placed on traumatic conditions. The section on muscles now includes a discussion on the physiology of squint, and the section on ptosis and its etiologic factors has been almost completely rewritten.

A National Health Service. By the Ministry of Health for Scotland. Reprinted. 8°, paper, 85 pp. New York: Macmillan Company, 1944. 75 cents.

This pamphlet describes and discusses the proposed comprehensive health service for England, Scotland and Wales. This plan will be put into effect on the termination of the war, and the purpose of this pamphlet is to examine the subject generally, showing what is meant by a comprehensive service and how it fits with what has been done in the past and what is being done in the present. The topics discussed include general administration, hospital and consultant service, general-practitioner service, clinic and other services, payment for the service and the application of the plan to Scotland.

Report of the Baruch Committee on Physical Medicine. For the Committee, by Ray Lyman Wilbur, M.D., chairman. 8°, paper, 120 pp. New York: Baruch Committee on Physical Medicine, 1944.

The committee recommends a plan for the sound development of physical medicine on a lasting basis. Various subcommittees have considered the subjects of teaching, basic research, clinical research, public relations, rehabilitation, hydrology and health reports, occupational therapy and body mechanics. These subcommittees presented special reports to the central committee, and that committee has recommended an immediate program and also an eventual program. The immediate program includes the organization of the central office with a governing board and an advisory board of experts in physical medicine and related medical fields, the establishment of fellowships and residencies in physical medicine, the promotion of teaching of and research in physical medicine in all approved medical schools, the promotion of wartime and postwar rehabilitation and the provision for preparation and publication of reports of the committee. The eventual program has to do with the promotion and advancement of physical medicine through various public channels, including the adoption of certain resolutions concerning projects of organizations on which the committee looks with favor. The reports of the subcommittees are printed in full.

Tropical Nursing; A handbook for nurses and others going abroad. By A. L. Gregg, M.D., M.Ch., B.A.O. (Dublin), D.T.M. and H. (Lond.), L.M. (Rotunda Hosp.), member of associate staff and lecturer to nurses, Hospital for Tropical Diseases, London, and lecturer on tropical diseases, Westminster Hospital Medical School. Second edition. 16°, cloth, 185 pp. New York: Philosophical Library, 1944. $3.00.

This small book has been written primarily for nurses in the field. There is a short chapter on personal hygiene in the tropics, followed by consideration of nursing in the various tropical diseases. There is also a chapter on the technics and special methods used in treatment. The last chapter is on the care of the eyes.

The Treatment of Peptic Ulcer. By George J. Heuer, M.D., professor of surgery, Cornell University Medical College and surgeon-in-chief, New York Hospital. Assisted by Cranston Holman, M.D., assistant professor of clinical surgery, Cornell University Medical College; and William A. Cooper, M. D., assistant professor of clinical surgery, Cornell University Medical College. 8°, cloth, 118 pp., with 2 charts. Philadelphia: J. B. Lippincott Company, 1944. $3.00.

This monograph is based on the case histories of 1204 patients with gastric, duodenal or marginal ulcers admitted to the New York Hospital for various reasons. The book is divided into two parts — medical treatment and surgical treatment. There is also a chapter on the incidence of malignant neoplasms, and another gives a survey of pertinent literature, with an appended bibliography.

Synopsis of Neuropsychiatry. By Lowell S. Selling. M.D., Ph.D., D.P.H., director, Psychopathic Clinic, Recorder's Court, Detroit, Michigan, associate attending neuropsychiatrist, Eloise Hospital, and adjunct attending neuropsychiatrist, Harper Hospital, Detroit. 12°, cloth, 500 pp. St. Louis: The C. V. Mosby Company, 1944. $5.00.

This simplified manual has been written for the student with the hope that it will serve him as a quick guide for diagnosis and treatment and provide a background for intensive review.

Psychiatry and the War: A survey of the significance of psychiatry and its relation to disturbances in human behavior to help provide for the present war effort and for postwar needs. Edited by Frank J. Sladen, M.D., physician-in-chief, Henry Ford Hospital, Detroit. 8°, cloth, 505 pp. Springfield, Illinois: Charles C Thomas, 1943. $5.00.

This book is made up of a collection of papers presented to a conference on psychiatry at the University of Michigan. It is a survey of psychiatry and its closely allied fields. The work is divided into five parts: the philosophy of psychiatry; research in psychiatry; psychiatry in the training, experience and education of the individual; psychiatry and the war; and review of the subjects already presented, which were summarized in two symposiums.

Infections of the Peritoneum. By Bernard Steinberg, M.D., director, Toledo Hospital Institute of Medical Research. With a foreword by Frederick A. Coller, M.D., professor of surgery, University of Michigan Medical School, and director, Department of Surgery, University Hospital, Ann Arbor, Michigan. 8°, cloth, 455 pp., with 45 illustrations and 21 tables. New York: Paul B. Hoeber, Incorporated, 1944. $8.00.

This new work on peritonitis embodies the experience of the author during the last eighteen years. The work is designed for the practitioner who is confronted with the task of arriving at a diagnosis and mapping out the therapy. Most of the book is devoted to the clinical aspects of infections of the peritoneum, and many new views in the developmental mechanisms, etiology, diagnosis and treatment of peritoneal infections are included.

Bacterial Infection: With special reference to dental practice. By J. L. T. Appleton, D.D.S., Sc.D., professor of bacteriopathology and dean, Thomas W. Evans Museum and Dental Institute School of Dentistry, University of Pennsylvania. Third edition, thoroughly revised. 8°, cloth, 498 pp., with 86 engravings and 5 plates. Philadelphia: Lea and Febiger, 1944. $7.00.

The primary purpose of this book is to aid the reader in forming a comprehensive concept of infection. The work is written primarily for dentists, and this third edition has been thoroughly revised and rearranged. New chapters on the ecology of the micro-organisms of the mouth, actinomycosis and osteomyelitis have been added. The work is divided into three parts: morphology, physiology and ecology of bacteria; infection; and special infections of the oral cavity.

Principles and Practices of Inhalational Therapy. By Alvan L. Barach, M.D., associate professor of clinical medicine, Columbia University College of Physicians and Surgeons, and assistant attending physician, Presbyterian Hospital, New York City. 8°, cloth, 315 pp., with 59 illustrations. Philadelphia: J. B. Lippincott Company, 1944. $4.00.

This new monograph is written for physicians who wish to understand the physiologic basis, as well as the technics, of inhalation therapy. The book opens with a short chapter on the historical and physiologic background, followed by a discussion of all the diseases in which the therapeutic use of gases is indicated; it concludes with methods and apparatus used in the treatment.

Physical Medicine in General Practice. By William Bierman, M.D., attending physical therapist, Mount Sinai Hospital, New York City, and assistant clinical professor of therapeutics, New York University Medical College. 8°, cloth. 654 pp., with 310 illustrations and frontispiece. New York: Paul B. Hoeber, Incorporated, 1944. $7.50.

This new textbook has been written for the practitioner in general and special fields of medicine. The work is condensed, covering all the agencies used in physical therapy and their applications to diseases of the various systems of the body. Historical references, as a rule, have been omitted, as well as extensive descriptions of the physics of light, heat and electricity.

One Hundred and Fifty Years Service to American Health. By Schieffelin and Company. 8°, cloth, 73 pp., with 30 illustrations and frontispiece. New York: Schieffelin and Company, 1944.

This small volume relates the interesting history of the oldest drug house in America, first founded in 1781 and still in active business in New York City, with a continuous history of one hundred and sixty-three years. The book is well done and contains a number of interesting illustrations. It is worthy of a place in all medical history collections.

A Dynamic Era of Court Psychiatry, 1914–1944. Edited by Agnes A. Sharp, M.A., Ph.D. 8°, paper, 149 pp., with illustrations. Chicago: The Psychiatric Institute of the Municipal Court of Chicago, 1944.

The Psychiatric Institute of the Municipal Court of Chicago was established on May 1, 1914. This small volume consists of a number of articles by the staff of the institute on the various aspects of the work of the department. The book has two functions: to record the history of the first thirty years of the institute, and to present scientific facts of court psychiatry.

Sexual Anomalies and Perversions: Physical and psychological development and treatment. By Magnus Hirschfeld, M.D., president of the World League for Sexual Reform, and director of the Institute for Sexual Research, Berlin. 8°, cloth, 630 pp. New York City: Emerson Books, Incorporated, 1944. $4.95.

This volume comprises a summary of the works of the late Dr. Hirschfeld and is compiled as a memorial by his pupils. The book was originally published in England, and the sheets have been imported and bound in the United States to supply the American professional public. The present work was originally planned by Dr. Hirschfeld as a textbook for those who need knowledge of sexual pathology. He died before he completed his work, and his pupils finished the book and prepared it for the press. The book is divided into five parts: The physical basis of sexuality; irregular sexual development and quantitative irregularities; deflections of the sexual impulse; sexual aberrations arising from fixations on component impulses; and other partial impulses. Because of its character the volume is restricted to the medical and legal professions, to ministers and to educators and special students in the fields of psychology, biology and sociology.

Female Endocrinology, Including Sections on the Male. By Jacob Hoffman, M.D., demonstrator in gynecology, Jefferson Medical College, and pathologist in gynecology, Jefferson Hospital. 8°, cloth, 780 pp., with 180 illustrations. Philadelphia: W. B. Saunders Company, 1944. $10.00.

This new treatise is divided into three parts: physiology of the endocrine glands; the clinical aspects of gonadal and reproductive endocrinology; and laboratory work. In presenting the clinical material, emphasis is placed on disturbances of functional organs. Diagnostic aids adapted for use in endocrine disorders are described. The hormonal preparations now available for the treatment of gonadal and reproductive disorders are described and tabulated, and their indications and contraindications are fully considered. Select bibliographies are attached to each chapter, and appended to the text is an index of names for all articles mentioned in the book.

Clinics. Vol. II: No. 5. (February 1944). Edited by George Morris Piersol, M.D., professor of medicine, Graduate School of Medicine, and professor of clinical medicine, School of Medicine, University of Pennsylvania, Philadelphia. 8°, paper, 266 pp., illustrated. Philadelphia: J. B. Lippincott Company, 1944. $2.00.

Simplified Diabetic Management. By Joseph T. Beardwood, Jr., M.D., associate professor of medicine, Graduate School of Medicine, University of Pennsylvania, physician to the Presbyterian Hospital, Philadelphia, physician-in-chief to the Department of Metabolic Diseases, Abington Memorial Hospital, Abington, Pennsylvania, visiting physician in charge of diseases of metabolism, Bryn Mawr Hospital, Bryn Mawr, Pennsylvania, and chief of the Metabolic Department, Philadelphia Hospital for Contagious Diseases; and Herbert T. Kelly, M.D., associate in medicine, Graduate School of Medicine, University of Pennsylvania, associate physician, Presbyterian Hospital, Philadelphia, and chief, Department of Medicine, Doctors' Hospital, New York City. Fourth edition. 12°, cloth, 172 pp., with 7 illustrations and charts. Philadelphia: J. B. Lippincott Company, 1944. $1.50.

This manual has been revised and brought up to date in relation to present-day conditions. Diabetic diets have been revised to conform to war and food-rationing regulations. Many of the chapters have been simplified, especially that on acidosis. There has been included a new chapter, which discusses the care of the diabetic woman during pregnancy. The manual is primarily for the diabetic patient to serve as a guide and daily source of reference.

Manual of Urology. By R. M. LeComte, M.D., professor of urology, Georgetown University School of Medicine. Third edition. 8°, cloth, 305 pp., with 60 illustrations. Baltimore: The Williams and Wilkins Company, 1944. $4.00.

The third edition of this students' manual has been carefully revised and brought up to date. Emphasis has been placed on traumatic lesions, which have increased as a result of mechanized warfare. A chapter on pain has been included, and the section on neurogenic bladder disorders has been rewritten and simplified.

The Medical Clinics of North America. New York Number (May, 1944). *Psychosomatic Medicine.* 8°, cloth, 262 pp., illustrated. Philadelphia and London: W. B. Saunders Company, 1944. $3.00.

The Medical Clinics of North America. Mayo Clinic Number (July, 1944). *Chemotherapy.* 8°, cloth, 239 pp., illustrated. Philadelphia and London: W. B. Saunders Company, 1944. $3.00.

NOTICES

BOSTON SOCIETY OF BIOLOGISTS

A meeting of the Boston Society of Biologists will be held in the Main Lecture Room of the Harvard Biological Laboratories on Wednesday, January 17, at 8 p. m.

PROGRAM

Transient Block of Conduction in Nerve Fibers Produced by Pressure or Ischemia. Dr. D. E. Denny-Brown.

Histochemical Reactions Associated with Basophilia and Eosinophilia in the Human Placenta. Drs. E. W. Dempsey and G. B. Wislocki.

The Argentaffin Cells of the Gastric Mucosa of Mammals. Dr. A. B. Dawson.

GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will be held at the Beth Israel Hospital on Tuesday, January 23, at 8:15 p. m. Dr. Paul Klemperer, of the Mount Sinai Hospital, New York City, will read a paper "Disseminated Lupus Erythematosus and Allied Conditions." Discussion by Drs. Monroe Schlesinger, Benjamin Castleman and M. Edward MacMahon will follow.

SOUTH END MEDICAL CLUB

The next regular meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, January 16, at twelve noon. The meeting will be devoted to a nutritional film in technicolor, which will tell of the detection and treatment of nutritional diseases. This will be discussed by Drs. Tom Spies and Norman Jolliffe and others.

Physicians are cordially invited to attend.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

The annual meeting of the New England Ophthalmological Society will be held at the Massachusetts Eye and Ear Infirmary, 243 Charles Street, Boston, on Tuesday, January 16, at 8 p. m.

Following the business meeting, which will include the election of officers, Dr. Edwin B. Dunphy will speak on the subject "Experiences in England." This will be followed by a paper "The Inheritance of Ocular Abnormalities" by Dr. R. Ruggles Gates, emeritus professor at the University of London.

NEW ENGLAND ROENTGEN RAY SOCIETY

The next meeting of the New England Roentgen Ray Society will be held at the Harvard Club, Boston, on Friday, January 19. There will be an x-ray conference at 4:30 p. m. At 8:00 p.m., a symposium on the topic "Osteomyelitis" will be presented; Dr. Edward B. D. Neuhauser will discuss "Roentgenologic Diagnosis" and Dr. Chester S. Keefer, "Methods of Treatment."

(*Notices continued on page xv*)

NOTICES (*Continued from page 62*)

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Thursday, January 18

Friday, January 19

*9:00–10:00 a.m. The History and Physical Examination of the Gynecological Patient. Dr. Louis E. Phaneuf. Joseph H. Pratt Diagnostic Hospital.

10:50 a.m. Syphilis — Present-Day Therapy. Dr. J. G. Downing. (Postgraduate clinic in dermatology and syphilis.) Dowling Amphitheater, Boston City Hospital.

Saturday, January 20

*10:00 a.m.–12.00 m. Medical staff rounds. Peter Bent Brigham Hospital.

Monday, January 22

*12:00 m.–1:00 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.

Tuesday, January 23

*12:15–1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital.

Wednesday, January 24

*9:00–10:00 a.m. Studies of Finger Capillaries in Neuroses, Epilepsy, and Migraine. Dr. Alfred Hauptmann. Joseph H. Pratt Diagnostic Hospital.

*12:00 m. Clinicopathological conference. Children's Hospital.

12:00 m.–1:00 p.m. Clinicopathological conference. Cambridge Hospital.

7:15 p.m. Graduate seminar in pediatrics. Children's Medical Service. Amphitheater 3A, Massachusetts General Hospital.

*Open to the medical profession.

January 16. New England Ophthalmological Society. Page 62.

January 17. Boston Society of Biologists. Page 62.

January 17. New England Society of Physical Medicine. Page xv, issue of December 21.

January 18. South End Medical Club. Page 62.

January 19. New England Roentgen Ray Society. Page 62.

January 20 and 21. Forum on Allergy. Page 638, issue of November 2.

January 23. Greater Boston Medical Society. Page 62.

February 3. American Board of Obstetrics and Gynecology. Page 696, issue of November 16.

February 8. Surgery Connected with the Liver and Pancreas. Dr. Joseph Tartakoff. Pentucket Association of Physicians. 8:30 p. m. Haverhill.

February 11. National Conference on Medical Service. Page 30, issue of January 4.

February 19. American Board of Internal Medicine. Page 436, issue of September 21.

May 22–24. Hotel Statler, Boston. Annual meeting of the Massachusetts Medical Society.

September 17. American Public Health Association. Page 752, issue of November 30.

District Medical Societies

PLYMOUTH

January 18. Brockton Hospital, Brockton.
February 15. Jordan Hospital, Plymouth.
March 15. Goddard Hospital, Brockton.
April 26. Toll House, Whitman.
May 17. Lakeville Sanatorium, Lakeville.

All meetings will be held at 11 a.m.

WORCESTER

February 14. Worcester State Hospital.
March 14. Worcester Memorial Hospital.
April 11. Hahnemann Hospital, Worcester.
May 9. Annual meeting.

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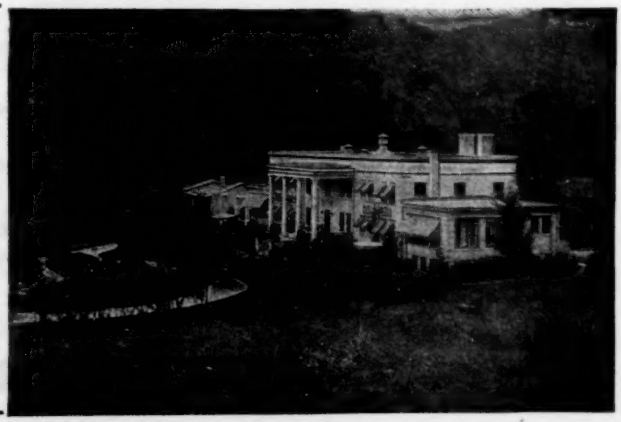

SHOULD VITAMIN D BE GIVEN ONLY TO INFANTS?

VITAMIN D has been so successful in preventing rickets during infancy that there has been little emphasis on continuing its use after the second year.

But now a careful histologic study has been made which reveals a startlingly high incidence of rickets in children 2 to 14 years old. Follis, Jackson, Eliot, and Park* report that postmortem examination of 230 children of this age group showed the total prevalence of rickets to be 46.5%.

Rachitic changes were present as late as the fourteenth year, and the incidence was higher among children dying from acute disease than in those dying of chronic disease.

The authors conclude, "We doubt if slight degrees of rickets, such as we found in many of our children, interfere with health and development, but our studies as a whole afford reason to prolong administration of vitamin D to the age limit of our study, the fourteenth year, and especially indicate the necessity to suspect and to take the necessary measures to guard against rickets in sick children."

*R. H. Follis, D. Jackson, M. M. Eliot, and E. A. Park: Prevalence of rickets in children between two and fourteen years of age, Am. J. Dis. Child. 66:1-11, July 1943.

MEAD'S Oleum Percomorphum With Other Fish-Liver Oils and Viosterol is a potent source of vitamins A and D, which is well taken by older children because it can be given in small dosage or capsule form. This ease of administration favors continued year-round use, including periods of illness.

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